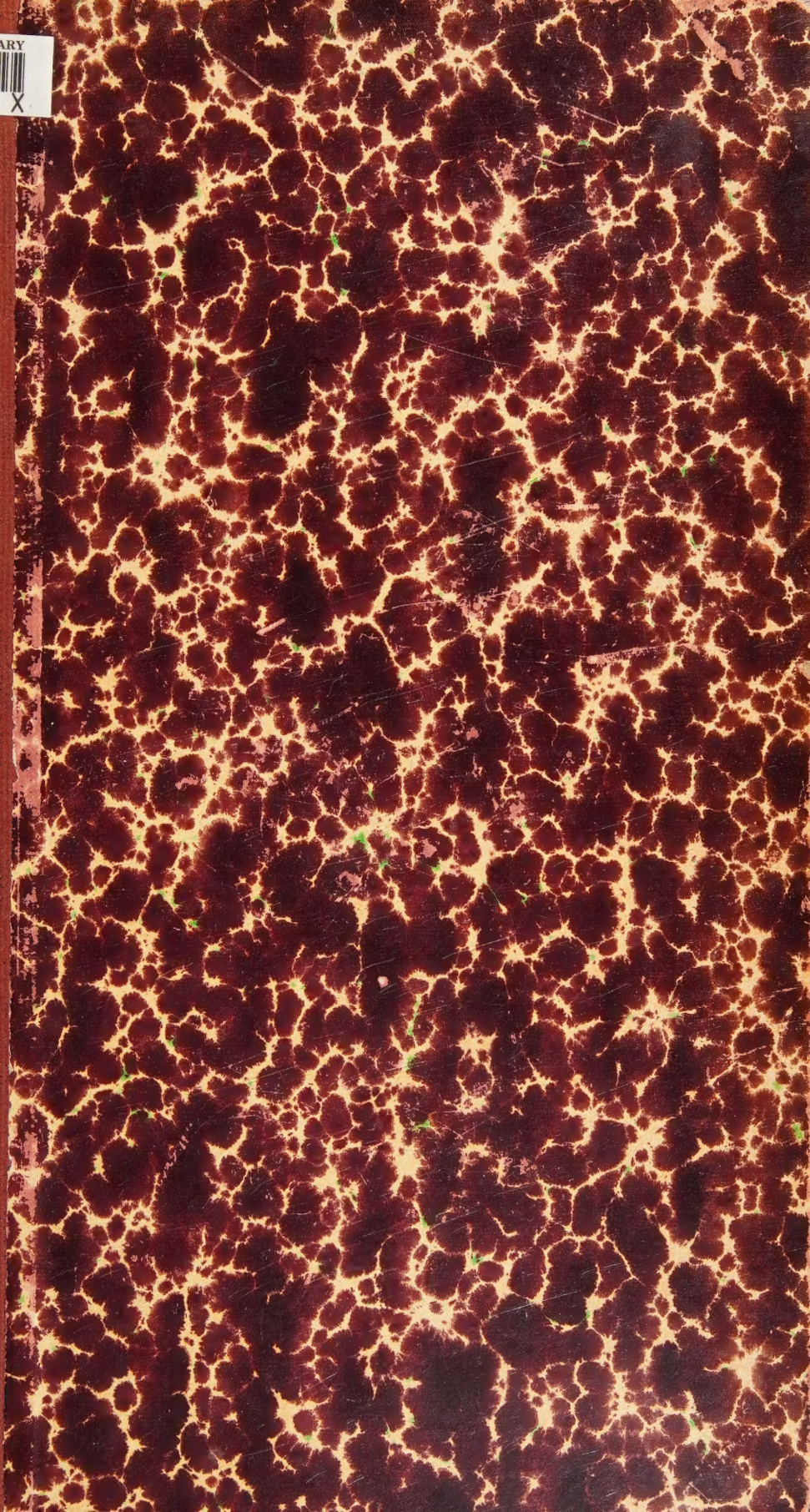
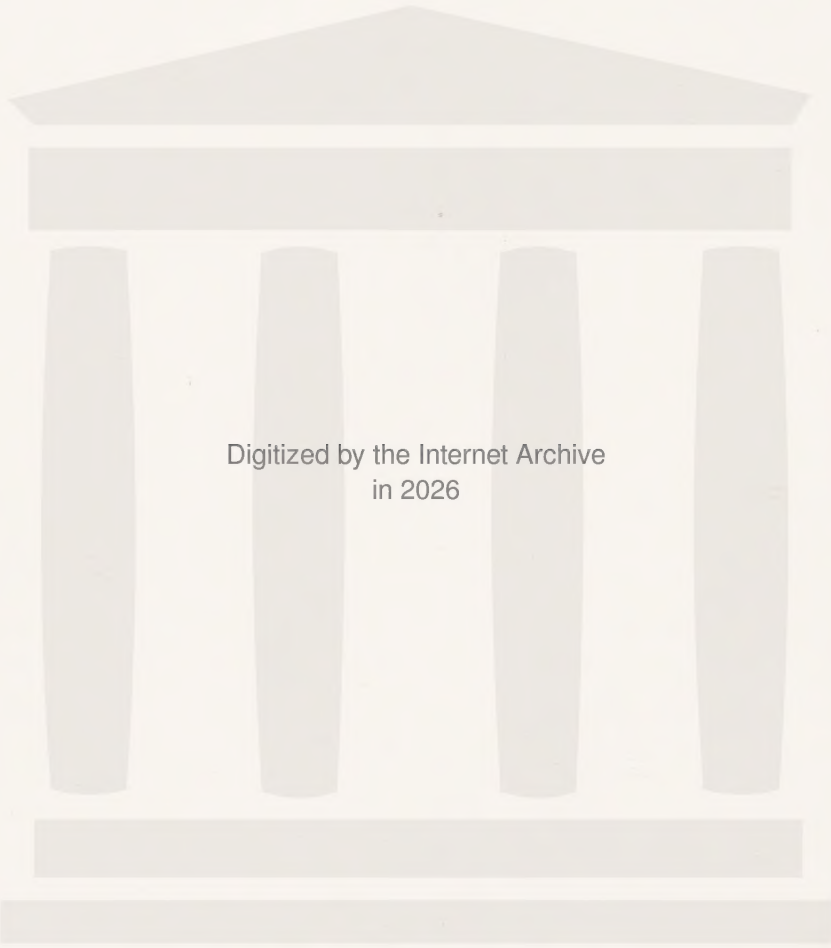


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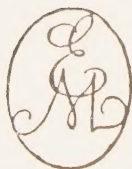
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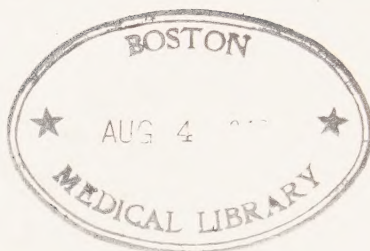
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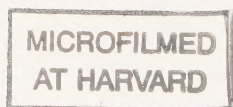
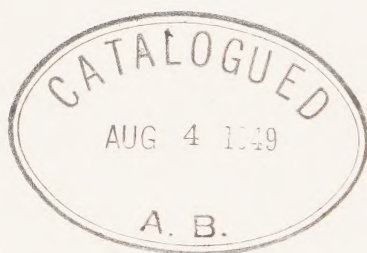
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EINAR MUNKSGAARD

On January 6, 1948, Einar Munksgaard, Ph. D., publisher, passed away. The *Acta Psychiatrica et Neurologica* owed him a great debt of gratitude.

In 1925, when a small number of Scandinavian and Dutch neurologists had decided to launch a neurologico-psychiatric journal containing original contributions in the English, French, and German languages, Einar Munksgaard, upon our application, at once came forward with great readiness and offered to publish the journal.

During the past 22 years Einar Munksgaard rendered invaluable services to this journal. His ability to establish international connections and his organising powers were pre-eminent, and thanks to these the *Acta Psychiatrica et Neurologica*, like all the other Scandinavian *Acta* published by his firm, obtained a circulation far beyond the boundaries of the Scandinavian countries.

By establishing connections with other journals on an exchange basis it was largely made possible to have papers from the *Acta* reported in these journals throughout the world.

In negotiations on financial and administrative questions concerning the *Acta*, Einar Munksgaard always showed great courtesy, judiciousness, and adaptability.

Einar Munksgaard was born at Viborg (Denmark) on February 28, 1890. He was trained as a bookseller at Viborg and afterwards for 6 years studied publishing methods in various European countries.

In 1917, in conjunction with Otto Levin, he founded what was at first a very unassuming business, Levin & Munksgaard, publishers and international booksellers. The firm rapidly grew and soon moved to the present premises at 6, Nørregade. After Levin's death in 1933, Munksgaard became sole owner of the bookselling business.

Munksgaard's firm has always been closely associated with science, more particularly medical science, somewhat less with fiction. Special credit is due to Einar Munksgaard for his publication of facsimile editions of Icelandic medieval manuscripts, the Iranian Avestas, and the *Corpus codicum Americanorum*.

He was on the board of directors of several concerns and a member of various committees connected with the publication of books. He himself wrote a number of books on similar subjects. In 1936 he was made Doctor honoris causa in the University of Reykjavik.

After Einar Munksgaard's death the firm is carried on by his two daughters, with Mr. Børge Heiring as managing director.

The Scandinavian Acta come under the special management of Mr. Erik Høeg, publisher.

Knud H. Krabbe.

ON THE NEUROMUSCULAR TRANSMISSION IN NORMAL AND MYASTHENIC SUBJECTS

BY

FRITZ BUCHTHAL and LISE ENGBÆK¹

(Institute of Neurophysiology, University of Copenhagen)

In patients with myasthenia gravis the injection of 20-40 mg. acetylcholine into the brachial artery produces a violent motor response, the fingers, hand and wrist going into sustained flexion for 10-15 secs (*Harvey and Lilienthal* 1941). Close arterial injection of corresponding amounts into normal human muscle produces a paresis (*Harvey et al.* 1941). Since also denervated muscle shows an increased sensitivity to acetylcholine compared with normal, the increased sensitivity of myasthenic muscle is considered to indicate that the latter has a diminished amount of transmitter substance (acetylcholine) available, so that a functional partial "denervation" is produced.

On the other hand the electrical response of myasthenic muscle to two stimuli with a short interval shows a reduction in amplitude of the second action potential, as is observed in partially curarized muscle (*Harvey and Masland* 1941). Therefore it has been concluded that myasthenic muscle corresponds to a partially denervated and a partially curarized muscle, and that both phenomena are due to a reduction in the release of transmitter substance (*Harvey et al.* 1942).

Mary Walker provided in 1938 indirect evidence of the presence of a curarizing agent in the blood of myasthenic patients and in 1944 *Wilson and Stoner* claimed to have demon-

¹ Working with a grant from the *P. Carl Petersen* and the *P. A. Brandt* Foundation.

strated a blocking action of serum from myasthenic patients on the neuromuscular transmission in the frog. The curarizing agent disappeared within 4 hours after withdrawal even when kept at low temperature. The negative results of *Cohen et al.* (1945), who did not find a decreased acetylcholine sensitivity in frog and leech muscle treated with prostigmine cannot be considered as contradictory evidence, since they stored the serum for 6 hours before the experiments.

As close arterial injection of small amounts of acetylcholine into cat and rabbit muscle produces a short tetanus-like contraction (*Brown, Dale and Feldberg* 1936), it seemed of interest to investigate the effect of corresponding amounts on human muscle. In the animal experiments the dosage after ligation of all but one artery to the muscle is 1-5 μ g. In a large dog under conditions corresponding to those applied to man, without anesthesia and ligation of arteries, we found that contraction occurs with between 20 and 100 μ g. acetylcholine. If the sensitivity of normal human muscle to acetylcholine should prove to differ from that previously found by *Harvey et al.*, it seemed that it would be worth while to compare it with the sensitivity of myasthenic muscle.

The presence of a curarine-like substance as found by *Wilson* and *Stoner* has been investigated in four cases of myasthenia; finally therapeutic results of treatment of myasthenia with diisopropyl-fluorophosphate are reported.

1. *Intraarterial injection of acetylcholine in man.*

Method: Injection was made into the brachial artery in the antecubital fossa.¹ After the needle (diameter 0.5 mm.) had entered the lumen, the artery was occluded by a blood pressure cuff placed on the upper arm, and the solution was injected within 2-3 sec., whereupon the pressure was suddenly released. The acetylcholine was freshly prepared before each experiment from acetylcholine hydrochloride ("Roche") dissolved in sterile 0.9 % NaCl. The volume of the injected fluid was 2 ml.

¹ Our thanks are due to *A. Tybjærg-Hansen*, M.D., who did part of the intraarterial injections.

Results:

In *normal subjects* acetylcholine produces a motor response of short duration immediately after the release of pressure. There is a localized flexion of 1-2 fingers or a flexion of all fingers or less frequently of the wrist as well. The differences are probably due to slight variations in the local concentration of the substance or in the threshold. The motor response is succeeded by the vasomotor effects. The arm begins to flush and sweat. Both reactions disappear within a few minutes. Generally there is no pain following the administration of a small amount of the substance.

The threshold dose of acetylcholine to produce a motor response was found in 23 normal persons to 200-300 μg . In women the threshold is slightly lower than in men (maximum 250 μg .), in one case the threshold was 150 μg . The muscle volume is probably of some significance, as the effective acetylcholine concentration will be dependent on the muscle mass and its vascularisation. The threshold for the vasomotor reaction was lower than that for the motor, but showed considerable individual variation.

Neurogenic and myogenic atrophy: In two cases of *amyotrophic lateral sclerosis* the acetylcholine threshold was considerably lowered (below 125 μg .), analogous to the increased acetylcholine sensitivity of *denervated muscle* (Brown 1937).

In two cases of *genuine muscular dystrophy* the acetylcholine threshold was found to be higher than the normal (450-550 μg .).

Myasthenic subjects: The investigations were carried out on 7 patients (6 females), three of them very severe cases. The threshold dose of acetylcholine is considerably higher in muscles from myasthenic patients than the 200-300 μg . found for normal muscle.

M. P. ♀ (daily dose of prostigmine 120-150 mg.). Prostigmine treatment was discontinued 18 hours before the experiment. The threshold dose of acetylcholine was approximately 400 μg . After intramuscular injection of 0.5 mg. prostigmine the threshold reached normal levels, 200 μg . producing a motor response. The patient was afterwards treated

with small amounts of di-isopropyl-fluorophosphate (D.F.P.) and retained the normal low threshold.

R. C. ♀ (Daily dose of prostigmine 270 mg.). Prostigmine was discontinued 3½ hours before the experiment. There was no motor response to 400 µg. acetylcholine. After injection of 0.5 mg. prostigmine 400 µg. was still ineffective, and 600 µg. produced slight fibrillations.

E. L. ♀ (daily dose of prostigmine 105-120 mg.). Prostigmine was discontinued 6½ hours before the experiment. The acetylcholine threshold was above 400 and below 800 µg. After intramuscular injection of 0.5 mg. prostigmine, 400 µg. produced a motor response. Several weeks later, when the patient was under the effect of D.F.P., the threshold was still between 300 and 400 µg.

V. Q. ♀ (daily dose of prostigmine 150-300 mg.). Tests were performed 3 hours after the last prostigmine medication. 200 µg. acetylcholine were without effect, 500 µg. produced a response.

G. H. ♀ (daily dose of prostigmine 150-180 mg.). The tests were made 18 hours after the last prostigmine medication. The threshold for acetylcholine was about 500 µg., doses between 250 and 400 µg. being without effect. After intra-muscular injection of 0.5 mg. prostigmine the threshold remained unchanged and even after a week's treatment with 2.0 mg. D.F.P. daily 400 µg. acetylcholine still did not release a motor response. Determination of the blood choline esterase showed total inhibition.

A vasomotor reaction to acetylcholine was hardly visible before injection of prostigmine, but after it the reaction persisted for several minutes. There was also a very pronounced local and general vasomotor reaction to acetylcholine after a weeks treatment with D.F.P. although the threshold for the motor response had not been affected.

K. K. ♂ (not yet treated with prostigmine). There was no motor response to 250, 500 and 750 µg. acetylcholine. After intramuscular injection of 0.5 mg. prostigmine 500 µg. acetylcholine produced a definite motor response and the vasomotor and sensory reactions, which had been weak and delayed were also considerably increased after prostigmine.

I. B. ♀ Thymectomy 16 months before the examination. Improved the first months after the operation (daily dose of prostigmine now 420-450 mg.). Prostigmine treatment was discontinued 8 hours before the experiment. Acetylcholine threshold was normal, 250 µg.

It is seen from the above that the threshold of myasthenic muscle to intraarterial injection of acetylcholine generally is above that of normal muscle. In 3 out of 5 patients the threshold was lowered after injection of 0.5 mg. prostigmine and remained at the lower level during treatment with small daily doses of D.F.P.

In one case (I. B.) which had been thymectomized, a normal threshold was found, although considerable doses of prostigmine still were necessary. Myasthenia was here preferentially localized to muscles of the face.

Although the thresholds of the motor response and the vasomotor reactions are not the same, we have the impression that larger amounts of acetylcholine are also necessary for the release of vasomotor changes in myasthenic than in normal subjects. After prostigmine the threshold for vasomotor reactions is lowered.

2. *Effect of serum from myasthenic patients on frogs nerve-muscle preparations.*

Method: The experiments were performed on the isolated m. semitendinosus with its nerve. In each experiment a control preparation was made, and it was treated with normal serum¹ during the experiment. The preparations were mounted in a double myograph for isometric contractions and the tension was recorded optically. The nerve was stimulated through silver electrodes and direct excitability of the muscle could be tested by applying the current throughout its length. The two preparations were always stimulated simultaneously either with single rectangular pulses (duration 5 ms) or with tetanic stimulation for 1-2 sec. (frequency 50/sec.). The intensity of the stimulus was approximately 3 times the threshold value. The tension of the contractions slowly decreased and it did not attain an absolutely constant value even after a long period of immersion in Ringer solution. Therefore the experiments were started before constant values were obtained as we always had an untreated preparation as a control.

Blood was withdrawn from patients with myasthenia gravis not under prostigmine treatment during occlusion of the circulation and after exercise of the muscles of the forearm until

¹ Acknowledgment is made to the *Ella Sachs Plotz Foundation* who has provided us with the centrifuge used in these experiments.

complete fatigue. Serum from normal persons was obtained either under the same conditions, or without occlusion and work (see results). The blood was kept on ice, and centrifuged at low temperature, the experiments were made less than 4 hours after the blood sampling.

Results: Torda and Wolff (1945) claimed that serum from normal cats obtained after active or passive movements has a curare-like action reducing the contraction of a frog's gastrocnemius by 20-40 per cent. In man serum taken after work performed during occlusion of the brachial artery had no such depressing effect as compared with serum from the resting extremity. Therefore, serum from myasthenic patients after work until fatigue was compared with serum from unfatigued normal persons. We tested the serum from 4 myasthenic patients, three of whom were severely affected by the disease.

In none of these cases did serum withdrawn after work until complete fatigue show the curare-like action described by Wilson and Stoner (1941).

3. *Treatment of myasthenia gravis with di-isopropyl-fluorophosphate.*

Since di-isopropyl-fluorophosphate (D.F.P.) has been found to cause a prolonged and irreversible inhibition of choline esterase several authors have used it in the therapy of myasthenia gravis. Gaddum and Wilson (1947) treated 3 patients with 0.5-2 mg. injected once daily. Two of them showed marked clinical improvement and their daily requirements of prostigmine fell, one had to abandon the treatment because of the muscarine-like action, which could not be counteracted with atropine. Comroe et al. (1946) used D.F.P. in the treatment of 7 patients with myasthenia gravis: In two it had little or no effect, 3 showed marked beneficial effects, and in 2 the effects were obscured by spontaneous remissions in the disease. In no case did the improvement equal that produced by prostigmine despite the fact that D.F.P. lowered the plasma choline esterase to zero.

As the D.F.P. treatment could be expected to have a more

prolonged effect due to the irreversibility of its action we tried D.F.P. on 3 patients.

The drug was injected intramuscularly once daily from a 2 %₀₀ solution in oil, the doses varying from 0.5-2.4 mg.

In all patients the treatment caused marked clinical improvement. In 2 out of 3 cases the patients could manage without prostigmine, and in the third case the prostigmine dose could be reduced.

The cases have already been mentioned as M. P., R. C. and E. L.

M. P. was first treated with 1 mg. D.F.P. daily, later with 0.8 mg.; 0.5 mg. had insufficient effect. After 8 days D.F.P. treatment and gradual withdrawal of prostigmine, she could carry on without the prostigmine, feeling quite well and free from aggravation of the symptoms during the night from which she had suffered while on prostigmine treatment. There were no toxic effects (electroencephalograms were taken in 2 cases and found to be normal). The serum choline esterase was reduced to 12-25 per cent. of the normal as measured by a biological test on guinea pig intestine. 10 months after discharge from hospital she is taking 1 mg. D.F.P., and can manage her work as a housewife. She has had slight transitory visual disturbances which disappeared after treatment with atropine.

R. C. was given 1 mg. D.F.P. daily, later increased to 2 mg. It was possible gradually to reduce prostigmine dosage to 105-120 mg. daily, but she did not show much improvement though she could now wash herself in the morning without prostigmine. No toxic symptoms which could with certainty be ascribed to D.F.P. were detected over an observation period of 4 months.

E. L. was given 1 mg. D.F.P. daily, gradually decreased to 0.5 mg. Within 5 days the prostigmine could be gradually withdrawn and she felt quite normal during most of the day. There were no toxic symptoms. Now 2 months after discharge from hospital she takes 60-105 mg. prostigmine daily + 0.5 mg. D.F.P. On this dose she is able to carry out her work as a housemaid which she was unable to do on prostigmine alone.

G. H. received 1 mg. and later 2 mg. D.F.P. daily. There was some benefit but the patient's information proved rather unreliable.

Discussion.

While in man intraarterial injection of large amounts of acetylcholine (20-40 mg.) has been shown to produce a decrease

in motor power (*Harvey et al.* 1941), small amounts produce a motor response comparable with that obtained in animal experiments. The paresis produced by large amounts is probably due to the blocking effect of persistent acetylcholine at the neuromuscular junction (*Buchthal and Lindhard* 1942).

In myasthenic subjects the acetylcholine threshold was found to be considerably raised, while intramuscular injection of prostigmine could in some cases bring it nearer to normal values.

A curare-like substance, the presence of which was demonstrated by *Walker* (1938) can account for the decrease in acetylcholine sensitivity of myasthenic muscles. This explanation is consistent with *Harvey's* findings on the action potentials of myasthenic muscles. In addition to this partial curarisation *Harvey et al.* (1941) who used rather large amounts of acetylcholine were forced by their results to assume a partial functional denervation. Our present observations make this assumption of a functional denervation unnecessary.

Detailed information concerning the curare-like factor in myasthenic serum is still lacking. We have been unable to confirm the findings by *Wilson and Stoner* (1944) of a blocking action of myasthenic serum on the neuromuscular transmission in the frog.

SUMMARY

In normal subjects the threshold for the motor response produced by injection of acetylcholine was 200-300 μ g.

In myasthenic subjects the acetylcholine sensitivity is considerably less. This applies both to the motor and to the autonomic reactions.

Reduction of the choline esterase by prostigmine or di-isopropyl-fluorophosphate lowers the raised acetylcholine threshold in myasthenic muscles.

These findings are in agreement with the assumption of a curare-like factor as the cause of the partial block in neuromuscular transmission in myasthenic subjects. However, the

blocking action of serum from myasthenic muscles on neuromuscular transmission in frogs could not be reproduced.

In two cases of amyotrophic lateral sclerosis acetylcholine sensitivity was considerably increased, while two cases of genuine muscular dystrophy showed a reduced sensitivity.

Three myasthenic patients treated with di-isopropyl-fluorophosphate showed marked clinical improvement.

The work has been supported by a grant from the *Michaelsen Foundation*.

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HERPES ZOSTER FOLLOWING OPERATIONS FOR FACIAL PAIN A CLINICAL INVESTIGATION ON 830 CASES

BY
LEOPOLD EPSTEIN

Herpes zoster (h. z.) in the face is a rather common phenomenon after operations for facial pain. As these operations are carried out not only at different places in the peripheral and central nervous system, but also differ quantitatively and, to some degree, qualitatively, possibilities have hereby been established which may be equalized with the experiment for a closer investigation of different conditions in connection with h. z., especially concerning the pathogenesis and location of the pathophysiological and pathologico-anatomical substrate.

The justification of this investigation is due to the fact that many fields in connection with h. z. are still incompletely revealed. This applies both to the etiology, the pathogenesis, and the location of the pathologico-anatomical substrate; but also other facts, e.g. the relation to other infectious diseases (herpes simplex, chicken-pox, encephalitis), the relation between the alterations in the nervous system and the cutaneous phenomena, the relation between symptomatic and idiopathic zoster are only incompletely elucidated. This investigation will preferably deal with the pathogenesis of postoperative h. z.

Concerning the questions of the innervation of the face, the conditions of facial pain, and the applied operations, reference is made to *Sjöqvist's* publications, (54, 55) where these questions

are more fully described. In the preface a survey is given of h. z. in general as it is thereby possible to elucidate several conditions in connection with postoperative h. z.

Survey:

The pathologico-anatomical substrate of herpes zoster in the central nervous system.

Von Bärensprung was the first to prove by clinical observations and postmortem investigations (1863) that h. z. may be due to a disease in the ganglia of the spinal nerves. These findings have since been confirmed by numerous investigators.

A significant contribution to the understanding of the histo-pathology of h. z. has been made by *Head & Campbell* (1900). In the state of eruption, infiltration of mononuclear cells, hemorrhage, and degeneration of ganglion cells and nerve fibres were found in the spinal ganglia. Degenerative alterations, interpreted as secondary to the processes of the ganglia, were found in the peripheral nerves, the posterior roots and columns. By eruption in the trigeminal area the same alterations were found in the Gasserian ganglion as in the spinal ganglia and degenerations in the tractus spinalis. The pathways and nuclei in pons were not affected. In the more serious cases the acute processes were followed by fibrous changes.

By the investigations of *Head & Campbell* the attention was to a too high degree turned to the spinal ganglia as the central substrate of the phenomenon. Later investigations (18, 2, 57, 34, 33) have proved that the inflammatory alterations can be more widespread; besides the peripheral nerves, anterior and posterior roots, the meninges and medulla spinalis can be attacked. In medulla the infiltration of mononuclear cells is especially localized perivascularly in the segment and the posterior column corresponding to the skin manifestations. Medullar processes without simultaneous affection of the ganglia have been described by *Nieuwenhuijse* (1914). *Wohlwill* (1924), who made the same observation, furthermore found radicular and peripheral inflammatory infiltration with intact or practically intact ganglion.

Clinical and histological investigations have shown that h. z. may also precede, be accompanied or followed by cerebral processes such as meningitis and meningo-encephalitis. In many cases it is difficult to decide if it is a question of essential zosterencephalitis or -meningitis, or a cerebral or meningeal inflammatory process of another etiology. So encephalitis lethargica with secondary zoster has been described (56, 59, 16, 43). Encephalitis interpreted as essential zosterencephalitis has been

observed by other investigators (52, 7, 53, 58, 50, 47, 38, 39). *Magnusson & Wohlfahrt* (39) found in 1 of their cases with h. z. in the trigeminal area, besides meningeal and cortical inflammatory infiltration, similar alterations in connection with degenerations in portio major, the spinal root and nucleus and in the pathways to the nucleus sensibilis pontis; but the motor nucleus in pons and the nucleus- and radix mesencephali were found intact. No safe alterations could be found at the sensory pontine nucleus.

That the pathologico-anatomical processes in h. z. cannot exclusively be localized to the spinal ganglia and the corresponding cerebral ganglia is evident from the fact that palsies have been observed clinically with h. z. indicating affection of cells or pathways of the motoric system (32, 56, 31, 65, 8). With zoster oticus palsy of the facial nerve may appear, and palsies of the ocular muscles have been described in connection with h. z. in the trigeminal area (22, 61, 29, 3).

From the preceding it will be seen that h. z. may be followed by inflammatory and degenerative alterations in the central and peripheral nervous system of varying intensity and extent. It may, therefore, often be difficult to decide where in the central nervous system the pathologico-anatomical lesion is localized which causes the cutaneous manifestation of the zoster. Many facts indicate that not only the ganglion of the first sensory neurone, but also other parts of the central nervous system are of importance as pathologico-anatomical and patho-physiological substrates. Our knowledge of the importance of these facts as regards the eruption of the cutaneous lesions is to some degree augmented through the frequent appearance of h. z. after operations for facial pain.

The Skin Lesion, Its Pathogenesis and Etiology.

A distinction is generally made between the two forms of h. z., the idiopathic form, a disease sui generis, probably produced by a specific filterable virus and symptomatic zoster, where a local or universal disease of another etiology is causing the zoster eruption, either by direct influence of the nervous system or indirectly by preparing the ground for the specific virus. Symptomatic h. z. may be seen with diseases of the vertebral column (fracture, tumour, tuberculosis), where the process gets into contact with or infiltrates the nervous system and by all cerebro-spinal diseases (encephalomyelitis, meningitis, tumour); but also infectious diseases outside the nervous system, e. g. pneumonia, and

universal intoxications (As, Bi, Co) may cause h. z. secondarily. In the group of secondary symptomatic zoster is included h. z. after operations for facial pain, where the causing factor is an interruption of nerve elements. Histologically there is no difference in the skin lesions by symptomatic and idiopathic h. z. (17, 43).

A detailed clinical and histological description of the skin lesions has already been given by *Head & Campbell*. They find a considerable amount of lymphoid cells, especially around the capillaries of the skin papillas below the vesicles and regional tender swelling of the lymphoid glands. Later investigators (21, 42, 35, 40) find similar alterations and consider the skin lesions primary and their histological character coordinated with the processes in the central nervous system.

According to *Wohlwill* pathologico-anatomical findings speak against the fact that the virus penetrates the skin and then moves centrally along the cutaneous nerves. Thus may be found infiltrative hemorrhagic neuritis without simultaneous affection of the fine cutaneous fibres. Besides it is a general experience that h. z. on the extremities is a rare phenomenon in spite of lesions on the extremities being more frequent than elsewhere on the body.

According to *Head & Campbell* skin lesions appear as a consequence of intensive irritation of the ganglion cells, which normally are of importance as regards the sensation of pain, especially the sort of pain produced by afferent visceral impulses through the sympathetic rami communicantes albi. In support of this supposition it is stated that the hyperalgesia which is followed by erythema and vesicles is similar to that often seen in connection with visceral pain, and that the ganglia which receive afferent impulses from viscera are most frequently attacked.

Kreibich (1909) and later *Wohlwill* (1924) believe h. z. to be a reflex phenomenon due to disturbances in the vasomotoric innervation of the affected skin area. The reflex may be released from any point of the afferent part of the somatic or sympathetic spinal reflex-arc. The conception harmonizes with the pathologico-anatomical findings. "Reflectorically" conditioned h. z. is described where skin lesions have occurred in connection with diseases of viscera innervated from the same segment as the affected skin area (4, 18).

According to *Staurmann & van d. Scheer* (1916) and *Hesser* (1924) the skin lesions are due to an irritation of the efferent sympathetic neurone. In support of that opinion *Hesser* indicates that the skin alterations are a vascular phenomenon, and that the sympathetic nerves innervate the blood vessels.

It is a prevalent opinion that the skin lesions are due to the destruction of special trophic neurones (*Gundersen*; and others); it is hereby mentioned that the disturbances of sensibility which may accompany the zoster eruption do not appear only on the herpes elements, but also

between these and outside the eruption. The herpes eruptions must therefore be due to lesion of special nerve elements which are considered of trophical importance.

Ingvær, who has given a detailed description of the morphology of the disease, believes that the skin lesions are secondary to irritative processes in the spinal ganglia caused by the inflammation, whereby highly active substances are released in the periphery, especially acetylcholine. The consequence is an aseptic inflammation in the skin with formation of vesicles. Thereby it is possible to explain that the zoster vesicles are sterile. Possibly the skin eruption is of importance in the immunization processes which prevent the development of more efflorescences.

It is possible that all forms of h. z. are due to a filterable virus; at least as far as the idiopathic h. z. is concerned, there are many indications that it is here a question of a specific infection. In support hereof it is indicated (I) that specific anti-bodies are proved to be present in the blood of zoster patients (7): (II) that the alterations of the central nervous system are of a specific type, (III) that there seems to be an etiological correlation between h. z. and chickenpox and possibly between h. z. and herpes simplex (40, 26, 52, 30, 44, 48). (IV) that the cells of epidermis of the skin lesions in h. z. just as with herpes simplex and varicella contain acidophile, intranuclear inclusions, indicating a virus disease (60, 36).

According to *Netter & Urbain* symptomatic h. z. is due to the same virus as idiopathic h. z. According to *Bedson* and *Knauer & Jaensch* the virus of all types of zoster is latent in the central nervous system and may be activated by nerve lesion.

It has not hitherto been possible with certainty to transfer the disease to healthy individuals and laboratory animals, a fact which, however, does not exclude that a filterable virus may be the causing factor.

Previous reports on herpes zoster after operations for facial pain.

The publications on h. z. following operations for facial pain are not very numerous. This certainly is due to the fact that previously the phenomenon has not been considered of much importance. After injection of alcohol in ganglion Gasseri, *Härtel* (1930) has seen h. z. in 10 % of 213 cases. Without indicating any figure, *Heymann* (1929) estimates that after almost every root-section herpes vesicles develop on the corresponding halves of the nose, cheek and lip. The appearance is explained as a

consequence of a trauma of the Gasserian ganglion and is due to a destruction of trophic nerves. According to *Peet*, h. z. occurs after sectioning of the sensory root as a consequence of an irritation of the ganglion during the exposure. In support of this supposition he indicates that h. z. is only developed in the area provided with fibres from that part of the ganglion, from which dura is removed. Furthermore, he mentions, *Cushing's* observation (1904) that where the ganglion is removed totally, h. z. do not develop.

According to *Dandy*, h. z. is developed almost as frequently after root section by temporal approach as by operation ad modum *Dandy*. II. z. is localized on the operated side, most frequently on the upper and lower lip and always from 24 to 72 hours after the operation. The cutaneous lesions are due to a destruction of a special trophic function of the nerve. This function should be different from that having relation to simple conduction of sensory and motor impulses. II. z. developed after operations on the trigeminal nerve is in every respect considered identical with h. z. from other causes.

Sjöqvist (54) mentions a case of atypical neuralgia, where h. z. occurred after tractotomy. Two years before temporal sub-total root section had been performed without permanent relief of the pain. The sensory disturbances after root-section had shown anesthesia-analgesia on the lower lip, hypesthesia-hypalgesia on the upper lip and cheek. After tractotomy h. z. appeared on the upper and lower lip, i.e. on areas to which the nerve conduction by temporal root section was respectively partly or totally interrupted. This is an experimental proof that the post-operative h. z. may be nuclear in origin and arise even when the interjacent nerve has previously been interrupted.

Rowbotham reports three cases of tractotomy, in one of which h. z. appeared in the postoperative course. After transitory light meningealialia h. z. developed at the end of the first week on the upper and lower lip. The sympathetic system, the facial nerve, and the motor root of the trigeminal nerve showed normal function. The tactile sensation was unaffected, the pain sensation abolished and the thermal sensation practically lost. *Rowbotham*

concludes: "a most interesting observation as herpes has always been thought to be due to injury of the Gasserian ganglion."

Estimate of the Material in Question.

The frequency of postoperative herpes zoster.

The material in question originates from the neuro-surgical departments of the Södersjukhus and the Serafiner Hospital in Stockholm. It includes 830 operations. On 50 patients 2 or more operations have been performed. The material is not suitable for an estimate of the zoster frequency after peripheral nerve sections and alcohol injections, the patients in these cases fre-

TABLE 1

*Frequency of herpes zoster after operations for the relief of facial pain. [Peripheral operations and alcohol injections not calculated in all cases *.]*

Operation		Number of opera- tions	Herpes zoster postoperat.	
			Number of cases	Percent.
Root-section		440	104	23.6
Dandy's operation		166	25	15.1
Tractotomy		111	8	7.3
Root- section, later on	Tractotomy	2	1	
	Sympathetic operations	4		
	Stellectomy & tractotomy	1		
	Dandy's operation	11		
Dandy's operat., later on	Root-section	12	2	
	Tractotomy	2	1	
	Tractotomy & Root-section	1		
Tracto- tomy, later on	Root-section	6		
	Dandy's operation	1		
Section of lemniscus medialis		1		
Intracranial section of 2nd branch		2		
Operat incl. alcohol- inject.	on the Gasserian gangl.	8	2	
	on the sympathetic system	4		
	on the peripheral branches	58	1	
All Cases*		772	143	18.5

quently being discharged from hospital before the appearance of herpes eruption might be expected.

As to the frequency of the different procedures, temporal root-section has been applied in 55.4 % of the cases. *Dandy's* operation (incl. *Olivecrona's* modification) in 21.4 %, tractotomy in 14 %, operations on the sympathetic system in 1 %, different operations on the Gasserian ganglion in 1 % and operations on the peripheral trigeminal branches in 7 %.

In Table 1 a survey of the herpes frequency is made. If peripheral nerve sections and alcohol injections are not included, postoperative h. z. is developed in 18.5 % of all cases. *This figure and all other figures which in this material refer to the herpes frequency, undoubtedly are the minimum figures, as probably not all cases of postoperative h. z. are mentioned in the journals.* The herpes frequency after temporal root-section, *Dandy's* operation, and tractotomy amount to 23.6 %, 15.1 %, and 7.3 %, respectively. Whilst the difference of the herpes frequency between temporal root-section and tractotomy is statistically significant, the difference between temporal root-section and *Dandy's* operation and between the latter and tractotomy is certainly considerable, but is not quite statistically significant, the difference being $8.5 \% \pm 3.4$ and $7.8 \% \pm 3.7$, respectively. Operations on the sympathetic nervous system have been performed in 9 cases without h. z. in the postoperative course.

At first *Dandy's* operation and later, owing to relapse, temporal root-section have been performed in 12 cases; in two of these cases h. z. appeared after the last operation. Unfortunately in one of the cases no complete testing of the sensibility had been made after the first operation. In the second case of *Dandy's* operation $\frac{2}{3}$ to $\frac{3}{4}$ of the root had been cut off; surprisingly normal sensibility was found in the face afterwards. 18 months after a subtotal, temporal root-section had been made, a single small bundle was preserved medially. 2 days later h. z. appeared on the lower lip. The sensation of all qualities was absent all over the operated half of the face.

Tractotomy preceded by temporal root-section has been executed in 2 cases; in 1 of these cases of h. z. appeared in the post-

operative course. This is *Sjöqvist's* case previously reported. Tractotomy preceded by *Dandy's* operation has also been performed in 2 cases. In the case where h. z. occurred after the tractotomy, *Dandy's* operation was performed subtotally by the application of a silver clip ad modum Olivecrona; afterwards normal sensibility was found in the areas of the first and second branch, reduced tactile sensation and lost sensation of pain and temperature in the third branch. After relapse 2 years later tractotomy was made. 2 days after the operation h. z. appeared on the lower lip, where sensibility for all qualities was reduced. The case cannot quite be compared with *Sjöqvist's* case, the first operation not leaving a totally lost sensibility in the later herpes area.

TABLE 2
*Frequency of herpes zoster after total and subtotal sections
of the trigeminal root.*

Operation	Number of opera- tions	Herpes zoster postoperat.	
		Number of cases	Percent.
Root-section			
Total	64	9	14.1
Subtotal	345	91	26.4
Dandy's operation			
Total	14	1	7.1
Subtotal	143	23	16.1

It is remarkable that h. z. both after *Dandy's* operation and after temporal root-section appears twice as frequently after subtotal as after total operations. (Table 2). The difference $12.3 \% \pm 4.9$ is not far from being statistically significant as regards temporal root-section. Unfortunately there are too few cases of *Dandy's* operation totally performed to permit a statistical estimate. Apparently h. z. appears most easily where part of the pathway is intact. From the difference found so much can up to now be concluded that ganglion Gasserii cannot exclusively serve as a releasing substrate for the development of h. z., but

TABLE 3

Frequency of herpes zoster after root-section, Dandy's operation, and tractotomy. Male- and female values compared.

Operation	Males			Females		
	Number of operations	Herpes zoster postoperat.		Number of operations	Herpes zoster postoperat.	
		Number of cases	Percent.		Number of cases	Percent.
Root-section	198	33	16.7	242	71	29.3
Dandy's operation	67	10	14.9	99	15	15.2
Tractotomy	51	2	3.9	60	8	13.3
All Cases	346	48	13.9	426	95	22.3

that h. z. may also be released from more central parts of the neurone system. In case the substrate of the herpes-releasing process be exclusively localized in the ganglion Gasseri, one might expect that the herpes frequency was practically the same with total and subtotal operations.

The female cases amount to little more than half of the material (55.1 %). Nevertheless, postoperative h. z. appears twice as frequently in the female cases as with men as regards the whole material, the percentages being 22.3 and 13.9, respectively (Table 3). The difference is statistically significant: $8.4 \% \pm 2.7$. It is not advisable, however, to draw too definite conclusions from these figures, the herpes frequency for the 2 sexes after *Dandy's* operation being almost of the same size.

The operative course in relation to herpes frequency.

It has been of interest to investigate whether or not especially difficult operations have had any influence on the frequency of postoperative h. z. The attention has especially been directed towards abnormally strong hemorrhage (meningea media-, dura-, sinus-, and carotis-hemorrhages) and more than usually pronounced traumatization of the nerve tissue (incl. repeated attacks on the nerve stem, several sections, etc.).

Table 4 is a survey of the appearance of operative hemorrhage

in the herpes group and in the herpes-free cases. Both with *Dandy's* operation and temporal root-section abnormally intense operative hemorrhage appears twice as frequently in the herpes group as in the herpes-free cases. The difference between the two groups with temporal root-section is $10.5 \% \pm 4.4$ and for all cases of root-section including *Dandy's* operation $9.6 \% \pm 3.97$. The difference thus is not far from being statistically significant. With tractotomy no operation is in any case characterized as especially hemorrhageous.

TABLE 4

Frequency of abnormally strong hemorrhages during the operation. The cases with postoperative herpes zoster compared with all other cases of the material.

Operation	Herpes-group			All other cases		
	Total number	Operative hemorrhage		Total number	Operative hemorrhage	
		Number of cases	Percent.		Number of cases	Percent.
Root-section	104	23	22.1	336	39	11.6
Dandy's operation	25	6	24.0	141	21	14.9
Tractotomy	8	0		103	0	

Repeated attacks on the nerve trunk have most frequently been performed by tractotomy [19 out of 111 cases in accordance with the special character of the operation]. In 8 out of the 19 cases h. z. has been developed in the postoperative course, which means that in all herpes cases after tractotomy repeated attacks have been made on the nerve stem. With temporal root-section several attempts of incision have been made in 4 out of 400 cases only, and in 1 of these cases postoperative h. z. occurred. With *Dandy's* operation repeated attacks have been made in 1 case, and afterwards postoperative h. z. has developed.

Where the central nervous system is strained abnormally through operation owing to hemorrhage or more intense traumatization, the soil seems more favourable for the development of postoperative h. z. than in cases of uncomplicated operations. This fact indicates that not only the section itself, but in certain

cases also another factor, possibly the hypothetical virus, plays a part for the occurrence of postoperative h. z.

The moment of eruption of the postoperative herpes zoster.

Exact information regarding the moment of the herpes eruption is known in 46 cases. Within 24 hours 41.3 % of the skin elements develop; within 48 hours 65.2 %; 82.6 % and 95.6 % within 3 and 4 days, respectively. In 1 case h. z. occurred immediately after the operation. In another case the skin lesion appeared on the sixth day, and finally in 1 case 3 months after the operation. It is, however, uncertain whether it is a question of postoperative h. z. in the last case. The rate of development for postoperative h. z. seems to be the same after the different operations.

The postoperative course and herpes zoster.

In Table 5 a survey of the postoperative course is taken. Complications in the shape of undesirable nerve lesions will be dealt with in a later chapter. In the group of uncomplicated postoperative course are found, not only cases which are in

TABLE 5

The postoperative course in the herpes-group compared with all other cases of the material (excl. peripheral operations).

The postoperative course	Herpes-group		All other cases	
	Number of cases	Percent.	Number of cases	Percent.
Febrile meningealialia	13	9.2	18	2.9
Meningeal hemorrhage	2	1.4	11	1.8
Non-febrile cerebral states	0		7	1.1
Extracerebral febrile states	5	3.5	41	6.7
" non-febrile states ...	1	0.7	15	2.4
Long fever (unknown etiology) ...	1	0.7	0	
Uncomplicated course	119	84.4	522	85.0
Total Number of Cases	141		614	

every respect normal, but all cases with subfebrile temperature and fever of some days' duration, on the supposition that the fever is not due to demonstrable cerebral or extracerebral causes. Uncomplicated postoperative course occurs just as frequently in the herpes group as in the herpes-free cases. Meningealialia owing to hemorrhage complicate the postoperative course with almost equal frequency in the 2 groups, between 1 and 2 %. Cerebral diseases of a not inflammatory character (thrombosis, embolia and hemorrhagia cerebri) do not occur in the herpes group, but in about 1 % of the group without postoperative h. z. Protracted high fever of undemonstrable etiology is found in 1 case in the herpes group.

Extracerebral febrile diseases have in the material in question hardly been of any importance as to the cause of postoperative h. z. It has not, however, been possible to exclude this possibility, the patients of the material consisting in the majority of elderly individuals, who after being confined to bed for a short time are rather predisposed to infectious diseases, especially phlebitis and hypostatic pneumonia. However, the frequency of extracerebral febrile diseases, particularly pneumonia, is only small in the material and even greater in the cases where h. z. does not appear (6.7 %) than in the herpes group (3.5 %).

As previously mentioned it has been proved that h. z. may be a manifestation of a meningo-encephalitis. It has therefore been of interest to examine the frequency of febrile meningo-cerebral complications in the material. Clinically demonstrable febrile meningo-cerebral complications in the postoperative course occur in 9.2 % in the herpes group, but only in 2.9 % in the herpes-free cases. The difference: $6.3 \% \pm 2.5$ is not quite statistically significant, but the findings might indicate that the postoperative h. z. in some few cases is caused by, or at least coordinated with a more generalized infectious process in the central nervous system, possibly as a result of an activation of the latent virus through the operation.

As the herpes frequency varies with the different operations it has been investigated if a similar difference might be found in respect of the frequency of postoperative febrile meningo-

TABLE 6

Febrile meningo-cerebral states in the postoperative course. The cases with postoperative herpes zoster compared with all other cases of root-section, Dandy's operation, and tractotomy.

Operation	Total number	Herpes-group		Total Number	All other cases	
		Febrile meningialia & cerebralialia			Febrile meningialia & cerebralialia	
		Number of cases	Percent.		Number of cases	Percent.
Root-section	104	6	5.8	336	1	0.3
Dandy's operation	25	2	8.3	141	9	6.4
Tractotomy	8	5	62.5	103	9	8.7

cerebral complications at the different operations. In Table 6 it will be seen that febrile meningo-cerebral complications both in the herpes cases and in the cases without h. z. appear most frequently after tractotomy, less frequently after *Dandy's* operation, and only rarely after temporal root-section. It is a striking feature that after tractotomy febrile meningo-cerebral complications are found in $\frac{2}{3}$ of all cases of postoperative h. z. Reservation must be made, however, for the fact that the percentage is calculated on the basis of very few cases.—There does not exist any correlation between the occurrence of febrile meningo-cerebral complications and the herpes frequency of the different operations.

Localization of postoperative herpes zoster.

The spontaneous h. z. in the face according to *Ingrar* is most frequently localized in the area of the first trigeminal branch. As he sees it, this is due to the fact that the nerve fibres of the trigeminal root and the ganglion cells of the ganglion Gasseri to the skin area in question are placed most superficially; as the virus of the spontaneous h. z. in *Ingrar's* opinion propagates in the subarachnoidal space, these nerve elements will be primarily attacked. However, it is no ordinary experience with operations on the sensory trigeminal root that the ophthalmic part encircles the other components of the root as a cuff; on the contrary the ophthalmic part of the root is situated most medially and is cut last by the total root-section.

According to *Frazier & Whitehead* (14) and *Frazier* (13) the sensory fibres of the trigeminal root are placed in parallel bundles with mutual localization in accordance with the position of the cutaneous zones. Section of the sensory root is followed by complete loss of all qualities of sensation. *Van Nuohuys* (46) and *Wilkins & Sachs* (63) find a considerable intermingling of the fibres of the 3 trigeminal branches.

As regards the conduction of the different qualities of sensation, it is *Dandy's* opinion that an arrangement of the fibres takes place already in the root so that the pain conducting fibres will be localized mainly in the lateral posterior part. These findings have not been confirmed by *Sjöqvist*.

TABLE 7

Localization of postoperative herpes zoster in 144 cases after operation for the relief of facial pain.

Operation	Localization of herpes						Not speci- fied
	Trigeminal zone					Outside trige- minal zone	
	I	II	III	I-II-III	II-III		
Root-section							
partial	2	25	25	1	36	1	1
total		2	3		4		
degree unknown		4					
later tractotomy					1		
Dandy's operation							
partial		6	2	1	13		1
total		1			1		
later root-sect. partial			1				
later root-sect. total .					1		
later tractotomy			1				
Tractotomy	1	3	2		2		
Explorat. exposure of							
Gass. ggl.					1		
Alcohol inject. in Gass. ggl.		1					
„ in periph.nn.			1				
Totals	3	42	35	2	59	1	2
Percentage	2.1	29.2	24.3	1.4	41	0.7	1.4

From Table 7 it is seen that postoperative h. z. after sub-total operations is mainly localized in the area of either the

second or third trigeminal branch or in the area of both these branches. In 12 cases with total root-section (incl. *Dandy's* operation) postoperative h. z. has been localized exclusively to the cutaneous area of either the second and (or) the third branch, and of 10 cases with h. z. after tractotomy the skin lesions have only in 1 case been localized to the area of the first branch. Only in 5 cases (3.5 %) the herpes lesion is found in the area of the first branch, or in addition to its localization in the area of the two lower branches, also in that of the first branch.

It is remarkable that postoperative h. z. in 4 out of 5 cases, where the lesion is found in the area of the first branch, has developed after subtotal procedures, where the ophthalmic part of the root is preserved. It is also remarkable that in the only two cases, where h. z. appears in the area of all 3 branches, there is no question of total, but of subtotal operations. In 1 of these cases after *Dandy's* operation the localization, however, is bilateral, indicating that at least the heterolateral lesion is part of a more general infection of the central nervous system. The same is certainly the fact in one case where the herpes eruption after subtotal temporal root-section is localized outside the trigeminal area to the cutaneous zone of the cervical nerves.—It is thus found that the kind and quantity of the procedure have no decisive influence on the localization of postoperative h. z.

Operative undesired nerve lesions and postoperative herpes zoster.

From Table 8 it is seen that lesion of the motor root of the trigeminal nerve appears in 25.7 % of the cases in the herpes group, but only in 14.4 % in the herpes-free cases. The difference: $11.3 \% \pm 3.9$ is almost statistically significant; it is, however, difficult to explain the importance of the fact. The lesion of the motor root may be an expression of the fact that the operation as a whole is more complicated, a condition that favours the development of postoperative h. z.—In this connec-

TABLE 8

Frequency of complicating nerve lesions following operations for the relief of facial pain.

Complicating Nerve—Lesions	Herpes-group		All other cases	
	Number of cases	Percent.	Number of cases	Percent.
Trig. Motor Root	37	25.7	99	14.4
Trig. Motor Root + Facial Nerve	4	2.8	27	3.9
Facial Nerve	9	6.2	51	7.4
Sympathetic System	1	0.7	16	2.3
No Nerve Lesion	92	63.9	493	71.9
Not Indicated	1	0.7		
Totals	144		686	

tion it should be mentioned that the motor root may conduct sensory fibres (37, 41), but naturally it is not possible to decide if this should be the case to a higher extent in the herpes group than in the herpes-free cases. As febrile meningo-cerebral complications, as previously shown, are a more common phenomenon in the herpes group than in the herpes-free cases, it is possible that lesion of the motor root in some cases is not due to section, but forms an analogy of the corresponding phenomenon sometimes occurring with spontaneous h. z.

Importance can hardly be attached to the facial nerve as regards the appearance of postoperative h. z. Lesion of the facial nerve appears almost with the same frequency in the two groups; it may be due to:

(1) section of the nerve in the face, (2) damage to the ganglion geniculatum by traction of the nervi petrosi superficiales, when dura is loosened from the inside of the skull, (3) damage at the brain stem by section of the sensory root (the possibility for this, however, is small, the distance between the two nerve stems being rather long), (4) inflammation or hemorrhage in the postoperative course. Apart from 2 cases in the herpes group where the operations were tractotomy and explorative exposure of the Gasserian ganglion and 1 case in the herpes free group, where the operation was tractotomy, all cases with lesion of the facial nerve appeared with temporal root-section and *Dandy's* operation.

Lesion of the sympathetic system appears in the herpes group only in one case, a very slight case, *Horner's* syndrome only being faintly marked; in the herpes-free group there are 16 cases of sympathetic lesion (2.3 %). The difference $1.6 \% \pm 0.86$ is not statistically proved, the condition, however, may indicate that an intact sympathetic nervous system is a necessary condition for the herpes eruption, the appearance of which might depend upon efferent impulses to the skin through the sympathetic nervous system.

Sensory conditions with postoperative herpes zoster.

Table 9 shows the sensibility in the herpes areas. Considerable difficulty is experienced in giving a complete survey of the sensibility in tabular form. Every single herpes area is classified separately; thus if h. z. in one case appears in the area of two trigeminal branches, the sensibility of each herpes area is indicated. Where the sensation of pain is reduced or lost, there is as a rule a corresponding degree of alteration as regards the thermal sensation. Hypesthesia-hypalgesia in connection with normal thermal sensation, however, is found in 2 cases and in connection with lost thermal sensibility in 1 case after *Dandy's* operation, subtotally performed. After tractotomy normal tactile and thermal sensation in connection with hypalgesia is found in 1 case.

Dissociated anesthesia in the herpes areas with normal or reduced tactile sensation in connection with lost sensibility of pain and temperature or a more reduced sensibility of pain and temperature than tactile sensation appears in 20 cases in all (cf. 5th, 6th, 7th, and 11th column of Table 9), with temporal root-section in 5 out of 131 cases (3.8 %), with *Dandy's* operation in 4 out of 36 cases (11.1 %), and with tractotomy in 11 out of 11 cases (100 %), in one of the last-mentioned cases the thermal sensation, however, is preserved.

Lost or reduced sensibility for all qualities is the most dominating alteration in the herpes areas and appears in 40.3 %

TABLE 9

The sensibility in the herpes areas after the different operations for the relief of facial pain. (Nat: sensibility normal, Hyp: sensibility lessened, An: sensibility lost.)

The sensibility in the herpes areas													
Sensitivity	Tactile sensation	Hyp	An	Nat	An		Nat		Hyp		Nat		Not stated
	Pain				Hyp	Nat	Hyp	Nat	Hyp	Nat			
	Temperature												
Operation	subtotal	45	55	4		2	1		4				3
	Root- total.....	1	11										
	section degree unknown	3	1					1					1
	later tractotomy												
	subtotal	16	4						3	1	1	2	4
	total		1						1	1			
	Dandy's later root-sect. subtotal												
	operat. later root-sect. total ...	1	1										
	later tractotomy							1					
	Tractotomy												
Explor. exposure gl. Gass.....			1				1	3	4			1	
Alcohol injection gl. Gass.....	1												
" peripher. nn..										1			
Totals.....		67	73	5		2	3	4	12	3	1	2	8
Percentage.....		37	40.3	2.8		1.1	1.7	2.2	6.6	1.7	0.6	1.1	4.4

and 37 % of the cases, respectively. Normal sensibility for all qualities is found in 5 cases, normal tactile sensibility in 13 cases, normal sensibility for pain in 8 cases and for temperature in 11 cases.—It is seen from the above that a lost, reduced, or preserved function of the ordinary sensory pathways for pain, temperature, and tactile sensation of the trigeminal nerve cannot be of importance in connection with the development of postoperative h. z.

Postoperative herpes zoster in relation to postoperative paresthesia and pain conditions.

As it is well-known that pain is a frequent, even if in most cases a transient accompanying phenomenon of spontaneous h. z., it has been of interest to investigate if postoperative conditions of pain and paresthesia appear more frequently where the operation is followed by h. z. than in the herpes-free cases. Such an investigation is justified from the fact that the zoster pain is practically uninfluenced by operative procedures. In other words, is postoperative h. z. a bad prognostical sign as regards relief of pain after operative procedures for facial pain?

In Table 10 the postoperative pain conditions are divided into (I) neuralgic pain, (II) paresthetic pain (besides ordinary paresthesia, dull continuous pain is included in this group), (III) relapse of pain, where the pain occurs after a free interval within 5 years after the operation, (IV) symptomatic pain (the primary disease in itself uninfluenced by the operation e.g. cancer). Statistically there is no demonstrable difference in the frequency of postoperative neuralgic and paresthetic pain in the herpes group and in the herpes-free cases. The frequency of relapse of pain seems to be nearly the same in the two groups, and persistent pain owing to symptomatic causes appears with exactly the same frequency.

It can be concluded from the above that the occurrence of postoperative h. z. does not affect the prognosis as regards complete recovery, as postoperative pain and relapse of pain do not

TABLE 10

The postoperative state in respect to pain. The herpes group compared with all other cases of the material (excl. peripheral operations).

The postoperative state in respect to pain	Herpes-group		All other cases	
	Number of cases	Percent.	Number of cases	Percent.
Neuralgic pain	9	6.3	41	6.5
Paresthetic pain	31	21.7	118	18.8
Symptomatic pain	5	3.5	21	3.3
Relapse of pain	7	4.9	42	6.7
Recovered	91	63.6	407	64.7
Totals	143		629	

appear more frequently where h. z. occurs after the operation than in the herpes-free cases. Unfortunately, the material is not suitable to decide whether the postoperative pain in the herpes group was of longer duration than where the operation was not followed by h. z.

Preoperative and postoperative herpes zoster.

In the material there are 9 cases of preoperative h. z., 4 of which occurred during the course of the facial neuralgia, whereas the other 5 cases are regarded as the cause of the neuralgia. Postherpetic neuralgia is thus a rare form of facial neuralgia (5 cases out of 830). *Cushing* has only 3 cases out of 332 facial neuralgias, *Frazier* (12) 1 case out of 520 and *Peet* 3 cases out of 400. The condition, however, is no doubt more frequent than is shown in a neuro-surgical material, the prognosis by operation with now generally applied methods being bad. Temporal root-section and explorative exposure of the ganglion Gasserii, performed in 3 and 1 cases, respectively, with herpetic neuralgia, had no effect on the pain. Finally, section of the second sensory neurone in lemniscus medialis was performed in 1 case, unfortunately with fatal result owing to thrombosis cerebri in the postoperative course.

Postoperative h. z. localized in the same area as the previous

preoperative h. z. appeared in 2 cases after total and subtotal temporal root-section and in 1 case after explorative exposure of the ganglion. Thus preoperative h. z. does not give any immunity against postoperative h. z., not even for the same skin area. Where h. z. appeared after explorative exposure of the ganglion, there was no injury of nerve tissue, but irritation of the ganglion had only been enough to release h. z. At the operation the third trigeminal branch was found atrophic, the dura sheaths over the ganglion had grown together and the ganglion showed inflammatory changes. In 2 out of the 3 other cases in which h. z. was regarded as the cause of the neuralgia and where temporal root-section was performed, alterations of the ganglion were likewise found, in one case atrophy, in the other inflammation.

Some considerations regarding the
pathogenesis of postoperative and
spontaneous herpes zoster.

On the basis of the histological findings by the spontaneous h. z. and from the experience gained through operations for facial pain it is now recognized that h. z. may be released from other parts of the central nervous system than the ganglion Gasserii. *Dandy* has thus, as previously indicated, shown that h. z. may be released just as easily after operations on the trigeminal root far from the ganglion in front of the brain stem as after temporal root-section; and *Sjöqvist*, as the first, proved experimentally that h. z. may be released from medulla spinalis by section of tractus spinalis. The present investigations have confirmed these findings, with the limitation, however, in respect of *Dandy's* publication that in my material h. z. appears almost twice as frequently after temporal root-section as after *Dandy's* operation.

As the fibres of the trigeminal root run essentially in parallel bundles and do not change their composition until after having penetrated into the brain stem, it is supposed that the more frequent appearance of h. z. after temporal root-section than

after *Dandy's* operation is due to irritation or traumatization of the ganglion Gasseri. Thus the ganglion Gasseri plays an important, but not decisive part for the development of post-operative h. z. The importance appears from a case in my material in which only the exposure of the ganglion was sufficient to provoke the eruption.

Whilst at the spontaneous h. z. there is a pathologico-anatomical substrate of an inflammatory and degenerative character, it is more uncertain if similar alterations appear by post-operative h. z. Here the section itself and its consequences at the place of operation (edema, hemorrhage) in connection with quickly occurring degenerative alterations form the pathologico-anatomical substrate. It cannot, however, be excluded,—as is indicated by the present investigations,—that in certain cases of postoperative h. z. similar alterations may be found as with spontaneous h. z. This is proved by (I) febrile meningo-cerebral complications, possibly provoked by the specific virus, appearing 3 times as frequently in the cases where postoperative h. z. occurs than in the herpes-free cases, (II) more intense traumatization of the tissue during the operation and abnormally strong hemorrhage, conditions which might be of importance for the activation of the latent virus, probably acting as a predisposing factor for the development of the postoperative h. z., (III) the localization of postoperative h. z. in rare cases appearing outside the area innervated by the interrupted nerve.

As regards the pathogenesis the dominating opinion is still prevalent that h. z. is due to lesion of especially trophic neurones. —Even if the pathologico-anatomical substrate of the spontaneous h. z. and the section of the postoperative h. z. may be localized at several places in the central nervous system and nevertheless give rise to herpes eruption, this does not in itself exclude that h. z. may be due to lesion of trophic nerves, and when postoperative h. z. appears more frequently after root-section than after tractotomy, it may be due to the fact that the localization of the trophic fibres are just so that they are preferably interrupted by root-section and to a slighter degree by tractotomy; but the difference in the herpes frequency be-

tween occipital and temporal root-section cannot be explained from the theory about trophic nerves, as the fibres in their radicular course are mainly running in parallel bundles and as regards quality do not alter composition until after penetrating into the brain stem. A section immediately behind the ganglion and near the brain stem should therefore result in same herpes frequency, if postoperative h. z. was caused by lesion or interruption of trophic neurones.

That the pathogenesis of h. z. is not so simple as the "trophic" theory indicates furthermore appears from the fact that subtotal root-sections twice as frequently give postoperative h. z. as total procedures. Should h. z. be due to a simple lesion of trophic neurones it is not possible to give any explanation of such a difference.

It has been proved that in no cases after total root-section and tractotomy h. z. appears in the corresponding total half of the face but only in a single or at the highest in the area of two trigeminal branches. After subtotal root-section, where usually less than one third of the ophthalmic part of the root is preserved, h. z. does not even appear in half of the cases in the area of both of the two lower trigeminal branches, just as it is shown that the localization in the area of the first trigeminal branch, indeed, even in the areas of all 3 branches, in the present material occurs only after subtotal operations. This missing correlation between the extension of the cutaneous manifestation and the degree of the root-section testifies against the fact that h. z. is due to lesion of trophic nerves.

In the herpes areas 5 cases with normal sensibility for all qualities are found. If h. z. is due to lesion of especially trophic neurones, these might be damaged separately without the other qualities being influenced. Such a possibility does not seem probable, but cannot, of course, be excluded, the nerves being actually cut by the operation.

Against the "trophic" theory and in favour of the pathogenetic considerations, which are to be mentioned later, speak *Sjögrist's* observations that tractotomy may release h. z. in a totally anesthetic area, to which the pathways are interrupted by

previous temporal root-section. It would be far-fetched to presume that the especially trophic nerves in this case were intact after the previous temporal root-section, whereas all other fibres to the skin area were cut. If a previous section (here temporal root-section) has damaged all fibres to a skin area and probably also the trophic ones, a renewed section by tractotomy will be unable to deprive the skin of its trophic innervation again and thereby cause h. z.

The fact that herpetic neuralgia cannot be cured by the hitherto applied operations incl. tractotomy suggests that the patho-physiological substrate of the disease may be localized more rostrally in the central nervous system, so that the pathogenesis of h. z. is no doubt more complicated than hitherto generally assumed. In this connection some pathogenetic suggestions made by *Frazier* (13) and *Sjöqvist* (55) regarding the genuine trigeminal neuralgia are to be dealt with briefly, as certain points of resemblance with the conditions with h. z. are found here:

Concerning the etiology of the genuine typical trigeminal neuralgia *Frazier* mentions some investigations of the sensibility preoperatively performed by *F. H. Lewy*. He measured the cronaxia with especially graduated stimuli. Ordinary investigations with cotton-wool sticks showed no alterations of sensibility, but now hyperesthesia-algesia was found in some cases, in other cases dysesthesia and hypesthesia. The alterations were not only found in the trigeminal area, but also on the body and extremities of the affected side. The findings might indicate that outside the sensory root and the ganglion Gasseri a pathogenetic factor may be present, e.g. in the thalamus. *Frazier* states furthermore that in one case of clinically typical trigeminal neuralgia with autopsia emollitions were found in the lateral and medial thalamic nucleus. The conclusion is that a pain condition of the sensory system may be explained by a higher centre being put out of function or damaged. Stimuli in the periphery, normally lying outside the border of perception, may now cause extremely violent pains.

Sjöqvist has compared the condition with trigeminal neuralgia with the condition of hyperirritability which may arise by mechanical compression of a peripheral nerve (*Zotterman*) or be released through reflex action, e.g. by acute abdominalia. With mechanical compression of a peripheral nerve one may speak about an "irritable focus" localized at the place of compression, the thick fibres being blocked, whereas the fine

ones are still functioning. Thereby tactile stimuli, normally remaining unconscious, may cause paroxysmal pains. With the reflex pain of acute abdominalia such an "irritable focus" might be localized in the 3rd or 4th cervical segment of the spinal cord (the phrenic nerve): with subminimal stimuli on the skin corresponding to the innervation areas of these segments an intensive pain in the shoulder may occur. With trigeminal neuralgia such an "irritable focus" may be localized in the peripheral nerve, in the root, in the nucleus spinalis and in the thalamus, so that the substrate of the disease may be different as regards localization and etiology, whereas the disease forms a unity as regards symptomatology.

The reason why *Frazier's* and *Sjöqvist's* considerations are mentioned here is that the trigeminal neuralgia and the herpes disease may be regarded as conditions of hyperirritability produced by organic alterations in the central or peripheral nervous system. Whilst *Frazier* localizes the organic alterations, forming the basis of the condition of hyperirritability, at a more highly localized centre (thalamus), *Sjöqvist* is of opinion that an "irritable focus" may be localized at different places. When tactile stimuli give rise to painful sensations, this may express that an "irritable focus" puts a superior centre in a condition of hyperirritability.

With h. z. (spontaneous and postoperative) it is a question of an organic alteration (sectioning, inflammation, degeneration), which may be different as regards etiology and localization; but the symptomatology (zoster blisters) is the same in all cases, probably as an expression of a common patho-physiological process. Whilst the organic alteration caused by operation is localized at the first neurone, there is considerable evidence of the herpes eruption being released from a more highly localized centre outside the sensory root and the ganglion Gasseri. The mechanism of the development of postoperative h. z. may rather be considered in such a way that the sectioning itself in connection with postoperative edema and possible hemorrhage at the place of operation acts as stimulus and puts a superior centre in a condition of hyperirritability, probably of short duration; hereby the patho-physiological basis of the zoster eruption and possibly of the zoster pain is formed. From this superior centre—presumably along sympathetic pathways—efferent impulses

are conducted to the skin and the mucous membranes and the eruption occurs. (Cfr. *Kreibich's* reflectory theory, page 16).

That conditions at the place of section (the degree of irritability) are no doubt of importance to the development of postoperative h. z. (the central condition of hyperirritability) appear from the fact, as previously shown, that operations complicated by abnormally strong hemorrhage during the operation are accompanied twice as frequently by h. z. as uncomplicated operations, just as stronger traumatization by the operation itself seems to be predisposing to the development of postoperative h. z. As postoperative h. z. is developed in the course of the first 4 days and not later, it may be an expression of the stimulus caused by the operation being only present for a short time.

As temporal root-section gives rise to postoperative h. z. more easily than *Dandy's* operation, this may be due to the fact that operations near the ganglion with the possibility of irritation of ganglion cells most easily release the condition of central hyperirritability. It is possible, however, that the reflectory process may be released directly via the ganglion Gasserii where this is damaged during the operation.

As subtotal operations more easily than total root-sections give rise to postoperative h. z. it may be explained by the centripetal part of the mechanism being furthered where part of the pathway is intact. For by subtotal operations not only the sectioning itself will act as a stimulus, but edema and hemorrhage at the place of sectioning may influence the preserved part of the root, so that the condition arises which *Sjöqvist* refers to by mechanical compression of a peripheral nerve. Such an "irritable focus" thereby becomes of importance as regards the development of the condition of central hyperirritability. The possibility must also be taken into consideration that the stimulus along sympathetic pathways may reach the periphery more easily when part of the trigeminal root is intact, the sympathetic fibres to a great extent following the somatic nerves to the periphery.

It is possible that the histological nature of the fibres plays

a part for the ease at which postoperative h. z. is released. In this connection it might be mentioned that a distinction is made between 3 kinds of fibres in portio major (26): (1) comparatively coarse fibres conducting tactile sensation mainly to the sensory pontine nucleus, (2) very thick fibres conducting proprioceptive stimuli afferently and forming tractus mesencephalicus, and (3) very fine fibres, the morphology of which has especially been elucidated by *Gasser & Erlanger; Adrian; Zotterman; Sjöqvist*. Conducting the sensations of pain and temperature the fine fibres in pons go particularly caudally to the upper part of the spinal cord, forming the tractus bulbospinalis.—The more frequent appearance of h. z. after root-section than after tractotomy might be due to h. z. being released most easily through lesion of the coarse fibres, which, as mentioned, only to a small degree run caudally in the spinal cord.

It is obvious to assume that the pathogenesis of spontaneous h. z. may be explained from the same point of view as has been set forth as regards postoperative h. z., so that by spontaneous h. z. it is a question of a reflectory process where the pathologico-anatomical alterations cause a condition of hyperirritability in ganglion cells of the sensory system (superior centres, possibly also the ganglion of the first sensory neurone), whereby the zoster eruption is released probably via sympathetic pathways.

With herpetic neuralgia there may be hypesthesia for weak tactile stimuli, whereas more intensive stimuli cause a painful paresthetic sensory sensation (*Sjöqvist*). Consequently, with spontaneous h. z., where it appears as herpetic neuralgia, there exists the same condition of hyperirritability, as is considered of pathogenetic importance for the development of postoperative h. z. The hyperpathia may sometimes be eliminated after root-section or tractotomy, whereas the dull permanent pain, forming the other component of herpetic neuralgia, is not influenced by the said procedures. This makes it probable that the pathologico-anatomical substrate of herpetic neuralgia is situated outside the first neurone, possibly nuclearly in the centre itself where the condition of hyperirritability is found, and from which the zoster is released. On the basis of the conditions of sensibility

and the bad results of operations on the first sensory neurone *Sjöqvist* assumes that the pathologico-anatomical substrate with herpetic facial neuralgia is probably situated either in the centre of perception of tactile stimuli: nucleus sensibilis pontis, or in the centre of receipt of pain: nucleus spinalis; possibly in still more superior centres, e.g. the nuclei thalami. It will be possible to elucidate this question more closely, when the possibility to a higher degree appears to operate on the second sensory neurone (*Dogliotti's* operation).

Is it justified to consider sympathetic nerves of any importance in the pathogenesis of zoster? If it is presupposed that h. z. is due to a condition of central hyperirritability, efferent impulses to the periphery will have no possibility of reaching the skin along other pathways than through the sympathetic nerves. In my material there is only 1 case of a slight sympathetic lesion in the herpes group, whilst in the other cases without h. z. 16 cases of sympathetic lesion are found, the percentages being 0.7 and 2.3, respectively. This fact might indicate that a sufficiently functioning sympathetic system forms a necessary condition for the development of h. z. Finally, it must be borne in mind that the skin eruption is a typically vaso-motoric phenomenon.

As postoperative h. z. only appears in about 20 per cent. (undoubtedly the minimum figure) after nerve section for facial pain, it may be supposed that another factor besides the section itself is of importance for the development of h. z. Thus as febrile meningo-cerebral complications are about 3 times as frequent in the herpes group as in the herpes-free cases, and as postoperative h. z. on rare occasions may be localized outside the area innervated by the cut nerve, this probably is an expression of the circumstance that the specific herpes virus is active in certain cases of postoperative h. z. Even if such an action in most cases cannot be proved clinically, the hypothesis cannot be rejected as improbable that the herpes virus must be present in all cases in order that postoperative h. z. can be developed. The herpes virus may be latently present with disposed individuals and then unfold its action where injured nerve tissue

in a certain pathologico-anatomical condition forms a favourable soil for activity. This applies to postoperative and other forms of symptomatic h. z.; with spontaneous idiopathic h. z. the virus itself presumably forms the pathologico-anatomical substrate. The special character of the skin lesion may be an expression of a specific action of the herpes virus.

SUMMARY

In 830 cases of facial pain the following operations have been applied: temporal root-section in 55.4 %, Dandy's operation (incl. Olivecrona's modification) in 21.4 %, tractotomy in 14 %, operations on the sympathetic system in 1 %, different operations on the ganglion Gasseri in 1 % and operations on the peripheral branches in 7 %.

(1) Herpes zoster (h. z.) appears in 143 out of 772 cases, i.e. 18.5 %. (Peripheral operations not included on account of a too short time of observation). The figure is undoubtedly the minimum figure (all cases hardly mentioned in the journals).

(2) The herpes frequency for all cases of the material, in men: 13.9 %, in women: 22.3 %. The difference: 8.4 % $\pm$ 2.7. With Dandy's operation, however, the difference is not significant.

(3) After temporal root-section, Dandy's operation and tractotomy the frequency of postoperative h. z. is 23.6 %, 15.1 % and 7.3 %, respectively. H. z. may be released from other parts of the central nervous system than from the ganglion Gasseri.

(4) The frequency of h. z. after subtotal and total root-section is for temporal root-section 26.4 % and 14.1 %, respectively, and for Dandy's operation 16.1 % and 7.1 %, respectively. The higher frequency after subtotal operations is nearly significant.

(5) Postoperative h. z. develops within 24 hours in 41.3 % of the cases, within 48 hours in 62.2 %, within 72 hours in 82.6 % and within 96 hours in 95.6 %.

(6) The kind and degree of the section have no decisive influence on the localization of postoperative h. z. There is no correlation between the extension of the cutaneous manifestation

and the degree of the section. It applies, however, to all operations (not only subtotal root-section) that the localization is preferably the area of the second or third or the second and third trigeminal branch.

(7) There is no uniformity in the sensibility to pain, temperature, and tactile sensation in the herpes areas. Lost, reduced, or intact function of the ordinary sensory pathways for pain, temperature, and tactile sensation is of no importance for the development of postoperative h. z.

(8) Lesion of the motor root of the trigeminal nerve occurs twice as frequently in the herpes group (25.7 %) as in the herpes-free cases (14.4 %), whereas lesion of the facial nerve appears almost with the same frequency (6.2 % and 7.4 %, respectively).

(9) Lesion of the sympathetic nerves appears in 2.3 % in the herpes-free cases and in 0.7 % in the herpes group (a very slight lesion). It is supposed that intact function of the sympathetic system plays a part for the development of postoperative h. z.

(10) Postoperative pain and relapse of pain is no more frequent where h. z. appears postoperatively than in the herpes-free cases.

(11) In the whole material herpetic neuralgia occurs in 5 cases. Root-section and tractotomy had no curative effect. In 3 out of 4 cases organic alterations of the ganglion Gasserii were found (atrophy and inflammation). Out of 9 cases with pre-operative h. z., postoperative h. z. appeared in 3 cases on the same skin area.

On the basis of the obtained findings it is assumed that the pathogenesis of the development of h. z. following operations for facial pain is not due to lesion of trophic nerves, as previously generally assumed; in favour of that supposition speaks: I. the difference in the herpes frequency after occipital and temporal root-section and after total and subtotal operations. II. The missing correlation between the extension of the skin lesions and the degree of sectioning. III. The appearance of skin eruptions in only about 20 per cent. of all operations. IV. Sjöqvist's case, where h. z. occurred after tractotomy in a totally

anesthetic area to which the interjacent nerve was previously cut.

The pathogenesis may rather be explained as a reflectory process, where the section with its consequences at the place of operation gives rise to a condition of hyperirritability in a superior centre, possibly nucleus sensibilis pontis or nucleus spinalis n. trigemini or nuclei thalami, from where, probably along sympathetic pathways, efferent stimuli go to the periphery.

It is possible that h. z. is most easily released through lesion of the coarse fibres which corresponds to the circumstance that h. z. appears more seldom after tractotomy than after root-section.

It is probable that the herpes virus in certain cases is of importance for the development of postoperative h. z.; in favour of this speak: (a) that h. z. may in a few cases be localized outside the area innervated by the cut nerve; (b) that operative complication in the form of abnormally intensive hemorrhage and more pronounced traumatization of the nerve stem seems to further the development of h. z.; (c) that febrile meningo-cerebral complications are more than three times as frequent in the herpes group (9.2 %) as in the herpes-free cases (2.9 %). The difference 6.3 ± 2.5 .—The theory is advanced that the herpes virus must be present for the development of all cases of h. z.

It is obvious to presume that the pathogenesis of other forms of h. z. may be explained from the same points of view.

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“CHOKED DISC” IN NEUROSYPHILIS

BY

SVEN ETHELBERG and VIGGO A. JENSEN

Swelling of the optic disc is no uncommon finding in neurosyphilis. It may be an initial symptom in an otherwise asymptomatic early meningeal or meningo-vascular syphilis, but it may also be seen at later stages.

Formerly this swelling was always called optic neuritis, especially by French authors, a rather misleading term, as it is very seldom accompanied by the characteristic functional disturbances, *viz.* defects of visual fields and reduction of visual acuity.

In recent years these changes have all been called choked discs, especially by English-speaking authors a name, in our opinion, equally misleading.

Where an optic neuritis with its functional disturbances can be excluded, we ought to use the purely morphological diagnosis: oedema of the optic papilla. This term is non-committal and designates only that the papilla is swollen due to oedematous infiltration, but leaves the question tumour *versus* basal meningitis open.

If a swelling of the disc is found in patients with neurosyphilis a ventriculography, in our opinion, should always be performed, notwithstanding that there are blurred, only slightly swollen papillae without measurable protrusion or typical choked discs of several diopters.

Only after ventriculography we can with certainty confirm or exclude the non-syphilitic affections that are of interest in

this respect. These are primarily the tumours of the frontal lobe which may give similar clinical symptoms, e. g. slightly pronounced psychical disturbances without neurological symptoms, midline-tumours only producing increased intracranial pressure and choked discs. The subdural hematoma as usual is one of the most difficult to preclude clinically. Also here the slowly developed and slightly pronounced psychical symptoms may be dominant. In brain abscesses the case history generally is so characteristic that a confusion should be out of the question; whereas the meningeal carcinomatosis with occult primary tumour may be clinically indistinguishable.

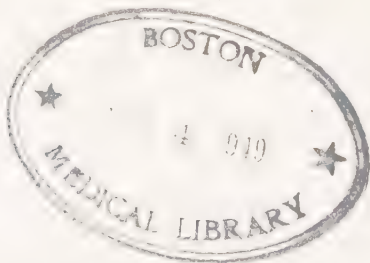
Meritt, Adams & Solomon advocate lumbar puncture as necessary to decide the differential diagnosis, even if they realize the danger inherent in this procedure, where an intracranial tumour is suspected.

In all cases, however, where a swelling of the disc of uncertain origin is present, we find lumbar or cisternal puncture contraindicated; the more so as positive Wassermann reaction in the spinal fluid is no conclusive evidence of the syphilitic origin of a given intracranial neoplasm, and as in cases of increased spinal pressure the question of meningitis *versus* neoplasm is still undecided.

Nor do we recommend the delay involved in diagnosing the case *ex jurantibus*.

Ventriculography, on the other hand, without increased intracranial pressure is a completely harmless procedure, and a routine treatment may be instituted immediately afterwards. If the intracranial pressure is increased, neurosurgical therapy may be inevitable and in this case ventriculography is as necessary a preliminary step as in all other intracranial procedures.

Does the ventriculography reveal a normal or slightly increased pressure without signs of tumour, it is natural to interpret the swelling of the disc as a collateral oedema to a cerebral meningitis and call it meningeal papilloedema (oedema meningeale papillae nervi optici). This, of course, does not prevent that the meningitis may at a later stage spread directly to the



optic nerve and here produce parenchymatous changes, *i.e.* a regular interstitial optic neuritis.

With an increased intracranial pressure without sign of tumour, it may be very difficult, even impossible, ophthalmoscopically, with certainty to distinguish between a "collateral meningeal papilloedema" and that produced directly by the intracranial pressure.

If the papillary tissue and the adjacent retinal zone are the site of an extraordinary oedematous infiltration, coinciding with slightly pronounced engorgement of the veins and few or no exudates and hemorrhages, this speaks in favour of a meningeal papilloedema.

If, on the other hand, a syphilitic basal meningitis gives rise to circulatory disturbances of the cerebrospinal fluid in the basal cisterns through a relative or total block, with consequently increased pressure, the papillary changes assume a more vascular character with pronounced engorgement of the veins and typical extravasates: a regular choked disc. Similar changes may be seen where the increased pressure is due to disturbances in the resorption of the cerebrospinal fluid in vertical meningitis or where it is due to large solitary gummatous tumours.

These syphilitics with swelling of the disc form a special therapeutic group. Apart from the antisiphilitic chemotherapy and possible fever treatment we may be forced to make a decompressive temporal craniotomy, to prevent the papilloedema from developing into secondary atrophy with reduction of visual acuity.

A temporal decompression is, however, no entirely indifferent measure, considering that it may lead to the formation of a musculo-cerebral cicatrix over the temporal lobe. We are inclined to perform it only if really urgent. In syphilitics with meningeal papilloedema and slight or no increase of intracranial pressure we find it justifiable to omit or postpone the decompression, even in the presence of pronounced papillary swelling, though, only on condition that these patients are under constant ophthalmoscopical control, so as to permit intervention, should the optic disc change its character in the direction of a regular

choked disc. If in the absence of tumour the intracranial pressure is distinctly increased and the papilloedema is of vascular character with hemorrhages and exudates, decompression should be performed immediately and routine treatment started.

If ventriculography indicates tumour, craniotomy should be made in all cases. Most often the tumour is of a non-syphilitic origin, but even if it is gummatus, which is very rare, it should be extirpated if possible, considering that *Alpers* maintains intracranial gummata to be resistant to chemotherapy. The opinion current until recently that gummata "evaporated" after antisiphilitic treatment is probably founded upon the fact that many cases of syphilitic meningitis with papillary swelling have been diagnosed as gummata, the effect of medicinal treatment on syphilitic meningitis being particularly striking.

In recent years we have had the opportunity in the Neurosurgical Department of the Municipal Hospital, Aarhus, to observe four of these patients whose case histories are reported below.

Case I: A 28 year old man, who since early youth had shown psychopathic traits. For these two years severe alcoholism. One year before admission syphilitic infection without any treatment at all. For one year increasingly frequent attacks of headache, shaped visual hallucinations, photisms in both visual fields and obscurations.

On admission he showed slight psychical deterioration, the speech was slightly slurred without definite dysarthria. Dubious right Babinski sign. *Ophthalmoscopy:* swelling of the disc $5/4$ diopters without extravasates but marked oedema and slight engorgement of the veins. Normal visual acuity and fields on both sides. Wassermann reaction on blood +++ . *Ventriculography:* Normal pressure; ventricular system slightly dilated without dislocation. Ventricular fluid: slight pleocytosis, proteins normal.

Treatment: No surgical treatment, later chemotherapy and hypertherm treatment. Spinal fluid after ventriculography: slight pleocytosis, proteins normal. Wassermann reaction +.

Diagnosis: Meningitis syphilitica, oedema meningeale nn. optic.

Case II. A 43 year old woman, who was infected with syphilis 24 years ago. In this period she was subjected to routine chemotherapy twice, last treatment twelve years before admission. For five years photisms. For two months headache, diplopia, intermittent loss of power in the right arm and stuttering.

Findings: Slight psychical deterioration, and slurring of speech. *Ophthalmoscopy*: bilateral swelling of the disc 2/2 diopters; one or two small hemorrhages, no exudates, marked oedema also in the adjacent part of retina, slight engorgement of the veins. Normal visual acuity and fields. Argyll Robertson's symptom positive. Spinal fluid: Increased pressure (5/600 mm.), medium pleocytosis and moderately increased protein values. Wassermann reaction on blood $\pm$, and on spinal fluid $\pm$.

Ventriculography: moderately increased pressure (2/300 mm.) ; marked dilation of the ventricular system without dislocation.

Operation: subtemporal decompressive craniotomy followed by hypertherm treatment.

Microscopy: bioptic tissue from right temporal lobe showed chronic (syphilitic) leptomeningitis, without changes in the cerebral tissue.

Diagnosis: Meningitis syphilitica. Oedema meningeale n. opt., stasis papillarum incipiens?

Case III: A 46 year old man, who denied syphilitic infection and never had any antisymphilitic treatment. For 20 years attacks of giddiness. For 10 years intermittent headache. For 5 years progressive psychical reduction. For 5 months photisms in both visual fields, severe nearly constant headache without nausea and vomiting.

Findings: Marked psychical reduction and definitely neurotic, hysterical reactions. *Ophthalmoscopy*: slightly swelled discs $<1/ <1$ diopter, marked oedema; no exudates or hemorrhages and only moderate engorgement of the veins. Slight functional

reduction of visual acuity of the right eye; left normal. Visual fields, being at first typical hysterical were later on normal on both sides. Wassermann reaction on blood +++.

Ventriculography: pressure 300 mm.; medium dilation of the ventricular system without dislocation.

Ventricular fluid: slight pleocytosis, proteins normal; Wassermann reaction: ++.

Operation: Subtemporal decompressive craniotomy followed by medicinal treatment.

Microscopy: Bioptic tissue from the right temporal lobe revealed no inflammatory changes in the meningeal and cerebral tissue.

Diagnosis: meningitis syphilitica (basalis?). Oedema meningeale nn. opt.

Case IV: A 53 year old woman. East Prussian refugee, who did not know anything about syphilitic infection and who had never been subjected to antisyphilitic treatment of any kind. For one year subjective reduction of vision, photisms, intermittent headache and giddiness, speech disturbances and rapid reduction of psychical powers.

Findings: Marked psychical reduction, euphory, loss of memory and concentration, the speech was slurred, but more detailed evaluation was not possible because of her East Prussian dialect.

Ophthalmoscopy: Swelling of the disc $4/3$ diopters, pronounced oedema, a few hemorrhages in resorption, no exudates, only slight venous engorgement. Normal visual acuity and fields. *Spinal fluid*: Pressure unknown, slight pleocytosis and slightly increased protein values. *Wassermann reaction* on blood + + +, on spinal fluid + + +. *Ventriculography*: Pressure 280 mm. Ventricular system slightly dilated and dislocated to the left. Ventricular fluid: slightly increased cell and protein values. *Operation*: After craniotomy over the middle part of the right hemisphere, extirpation of a $5 \times 6 \times 2$ cm. granuloma over the middle of the convexity, following the pial recesses deep down between the convolutions; all over the convexity of the

right hemisphere a 3 mm. woolly thickening of the meninges was found. Postoperatively she was subjected to routine treatment.

Diagnosis: Gumma intracraniale, meningitis syphilitica verticalis. Oedema meningeale nn. opt., stasis papillarum incipiens.

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EIN ORTHOTISCHES (LORDOTISCHES) KAUDASYNDROM

VON

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Amsterdam.

In dieser Mitteilung möchte ich das Interesse wachrufen an einem Krankheitsbild das ich bisher im Schrifttum nicht vorgefunden habe. Ich bin dem in der Überschrift erwähnten Syndrom während meiner neben allgemein-chirurgischer Betätigung ein hergehenden Beschäftigung mit der Neurochirurgie nunmehr zweimal begegnet.

Vor etwa einem Jahre meldete sich bei mir ein Mann in vorgerücktem Alter mit Gebbeschwerten: nach ungefähr zehn Minuten Gehen spürte er jedesmal eine Taubheit beider Beine, namentlich der Unterschenkel, die aus den Füßen herafzusteigen schien. Das Gehen wurde dabei unsicher und schliesslich musste er sich setzen, da die Muskelkraft der Beine nachliess. Dasselbe ereignete sich beim Stehen. Diese Erscheinungen waren nicht von Bein- oder anderen Schmerzen begleitet, auch nicht von anginösen Brustbeschwerden. Sie lösten sich beim Sitzen.

Die anamnestisch etwas funktionell anmutende Anästhesie erwies sich bei der Untersuchung als segmental begrenzt, voll ausgebildet umfasste sie die Segmente L.3 bis 5, sowie die Sakralsegmente. Keine Dissoziation. Motorisch ergab sich eine allgemeine Parese der Beine. Die im freien Intervall schon sehr niedrigen Sehnenreflexe fehlten im anästhetisch-paretischen Anfall der auch die willkürliche Miktion aufhob. Durchblutungsstörungen waren nicht vorhanden. Die Ataxie der Beine war nur im Anfall vorhanden. Im freien Intervall ergab die Unter-

suchung fast gar nichts: eine leichte Hypästhesie der anterolateralen Unterschenkelseite. Äussere Umstände gestatten damals nicht die (klinische) Lumbalpunktion und die Myelographie zur weiteren Klärung des als neurologisch bewerteten Falls. Ohne Laminektomie siedelte der Patient um, entzog sich weiterer Behandlung nach vervollständigter Untersuchung. Was aus ihm geworden ist habe ich nicht ausfindig machen können.

Ich wäre an diesem Fall sonderbarer Nervenpathologie wohl weiter vorübergegangen, hätte ich nicht seitdem einen ähnlichen, zweiten Fall in jeder Hinsicht untersuchen und operativ heilen können.

In letzter Zeit kam ein sechzigjähriger Herr zu mir. Nach mehr als zehn Jahre zurückliegendem »rheumatischem« Ischias mehrjähriger Dauer hatte er seitdem andersartige Beschwerden. Nach etwa viertelstündigem Gehen oder Stehen trat eine besonders an der Vorderseite der Beine aufsteigende Taubheit in die Erscheinung, ohne vorangehende Schmerzen. Stehen und namentlich Gehen wurde dabei unsicher, später gesellte sich Muskelschwäche hinzu. Zur Behebung der Beschwerden genügte jedesmal sich setzen; sich hinlegen war nicht erforderlich. Die Erscheinungen konnten durch Gehen oder Stehen beliebig hervorgerufen werden, waren im Lauf der Jahre unzählige Male vorgekommen, und wieder rückgängig geworden. Eine von dem Patienten zweifelsohne gefürchtete Verschlimmerung war in den letzten Jahren nicht eingetreten. Vielleicht war das linke Bein etwas stärker beteiligt als das rechte. Sonst wurden keine Beschwerden — namentlich keine Harn- und Sexualstörungen — geklagt.

Bei näherem Nachfragen ergab sich dass die Beschwerden beim Radfahren nicht eintraten und das örtliche Kältesensation nicht hinzugehörte. Es versteht sich dass meine Gedanken bald Abstand nahmen von einer kreislaufbedingten Ursache etwa im Sinn der Claudicatio — Anoxämie: die Beschwerdefreiheit beim Radfahren wäre mit derselben nicht vereinbar und die Entstehung der nämlichen Beschwerden beim Stehen verträge sich schlecht mit einer Durchblutungsstörung. Somit wandte mein Interesse sich einer etwaigen neurologischen Ursache zu.

Übrigens hat die »innere Untersuchung nichts Besonderes, auch keinen Hochdruck, aufgedeckt. Es ist zu unterscheiden zwischen der neurologischen Untersuchung im beschwerdefreien Stadium (Intervall) und im »Anfall« d.h. bei manifesten anästhetisch-paretischen Erscheinungen beim Stehen und Gehen.

Ich werde nur die unbedingt notwendigen, meistens pathologische Tatsachen anführen.

Die neurologische Untersuchung im beschwerdefreien Intervall ergab nur sehr wenig. Oberhalb der Leistenbeugen war alles in Ordnung. An den Beinen waren die Patellarreflexe zwar nicht abwesend — vom Internisten allerdings als fehlend vermerkt — aber doch sehr niedrig. Der linke Achillessehnenreflex fehlte. Lasègue nicht vorhanden. Besonders am linken Unterschenkel zeigte sich Hypästhesie an der Streckseite sowie am fibularen Rande. Der Vergleich beider Beine zeigte keine unzweifelhafte Differenz der Muskelkraft, des Tonus und des Muskelvolums. Keine Ataxie. Am Perineum war nichts abnormes zu vermerken. Bis auf den fehlenden Lasègue somit ein Befund nicht unähnlich demjenigen der neurochirurgischen Ischias.

Die neurologische Untersuchung nach genügend langem Stehen oder Gehen deckte mancherlei auf, es handelte sich jedoch nicht um einen konstanten Befund. Je länger der Patient gegangen oder gestanden hatte umso mehr wich der Befund vom Normalen ab. Nach einiger Zeit wurde der Gang unsicher, mit tabetischem Gepräge, zunächst ohne Kräfteverlust. Das Aussehen des Patienten verfiel dabei offensichtlich, schliesslich musste er sich setzen, da die Muskelkraft erlosch. Örtliche Anämie, Zyanose oder Kälte fehlen auch dann noch.

Zunächst war eine nicht-dissoziierte Anästhesie anterolateral an den Unterschenkeln vorhanden die nicht bis über das Knie hinaus heraufreichte. Später erstreckte sich die massive Anästhesie vorn bis etwa ein Drittel des Oberschenkels oberhalb des Knies während an der Hinterseite eine Hypästhesie den ganzen Oberschenkel, das Perineum und den angrenzenden Teil des Gesässes einnahm. Es handelte sich somit schliesslich um Anästhesie der Dermatome L. 3 bis 5 und um Hypästhesie der Sakraldermatome. Der Tiefensinn hatte stark gelitten, war schliesslich

praktisch verschwunden: grobe Ataxie. Die zunächst vorhandene mehr oder weniger generalisierte Parese der Beine hatte sich nahezu zu einer Paralyse — die Adduktoren ausgenommen — verschlimmert. Sehnen- und Analreflexe waren verschwunden. In diesem Zustande der Anästhesie und schlaffen Parese war dem Patienten die willkürliche Miktion noch möglich. Es han-



Abb. 1 a.

Anästhesie im Anfangsstadium, Radikularsyndrom.

delte sich somit um ein reversibles, zunächst radikuläres Syndrom aus welchem schliesslich ein inkomplettes Kaudasyndrom entstand. Vielleicht konnte der Patient die zur Entstehung des Syndroms erforderliche Haltung nicht lange genug aushalten um ein vollständiges Kaudasyndrom hervorzubringen.

Der Liquorbefund in der Zyste war normal, unten war der Eiweissgehalt kaum als Beweis einer Liquorsperre anzusprechen.

Es wurde noch einige Versuche vorgenommen. Im Knien mit gestrecktem Rücken entstanden die nämlichen Beschwerden. Die Bauchlage, auch die reklinierte in einer Hängematte — wie bei der Böhlerschen Wirbelbruchbehandlung — liess keine Symptome aufkommen.

Was ist nun dem Gehen, Stehen und Knien gemeinschaftlich



Abb. I b.

Anästhesie im Schlusstadium, Kaudasyndrom, ein Segment höher heraufreichend.

im Gegensatz zum Sitzen, Radfahren und Liegen? Es ist offenbar die Unterstützung der belasteten Wirbelsäule mittels der *Tubera ischii*, sonst fehlt entweder die Belastung oder die Stütze wird durch die Femurköpfe in den *Acetabula* geleistet, welche die Beschwerden verhüten. Das Stehen u. s. w. mit weiter vorn stattfindender Unterstützung beschwört die Symptome des Kaudasyndroms herauf: gemeinschaftlich ist die Streckung,

Lordosierung der belasteten Wirbelsäule, namentlich des Lendenteils, in der aufrechten, nicht sitzenden Haltung. Es handelte sich bei meinen Patienten somit um ein lordotisches, orthotisches Syndrom zu dem die Belastung miterforderlich ist. Darin liegt ein Gegensatz zur lordotischen Albuminurie, zum ptotischen renalen Hochdruck. Bei der Erwägung der in Betracht

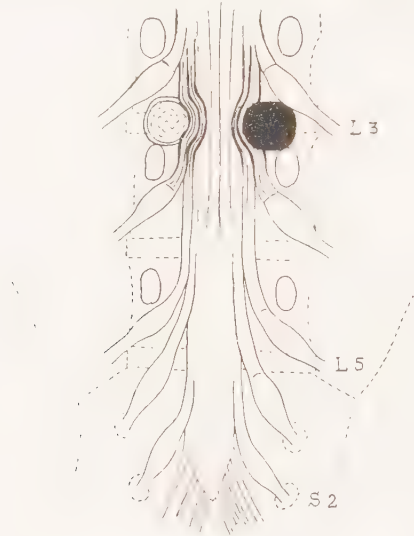


Abb. 2 a.

Vom Radikular- zum 1. Segment höher heraufreichenden Kaudasyndrom.

kommenden Ursachen des beliebig reversibelen Kaudasyndroms infolge Belastung und Lordosierung, Orthostase käme ein Angiom des Spinalkanals m. E. wegen der massiven Erscheinungen kaum in Betracht. Dann kommt die Reihe wohl an die Diskusprotrusion, Hernia nuclei pulposi in weitestem Sinn. Die gewöhnliche Symptomatologie der Diskushernie weicht allerdings sehr ab vom Vorstehenden in welchem von Schmerzen kaum die Rede war. Remissionen und Exacerbationen anlässlich spezieller Ursachen mechanischer Art sind allerdings in der gewöhnlichen Diskussymptomatologie etwas keineswegs aussergewöhnliches. Ein Einfluss des Hustens, Niesens und Pressens war bei meinem Patienten nicht vorhanden.

Bei der durchschnittlichen Diskushernie handelt es sich nur um ein Radikularsyndrom, es sind immerhin mehrere Diskusläsionen als Ursachen stabiler Kaudasyndrome beschrieben worden (*Verbrugghen*). Remissionen und beliebige Rezidive orthotischer, lordotischer Herkunft aus irgendwelcher Ursache heraus habe ich im Schrifttum nicht gefunden, auch nicht ausserhalb

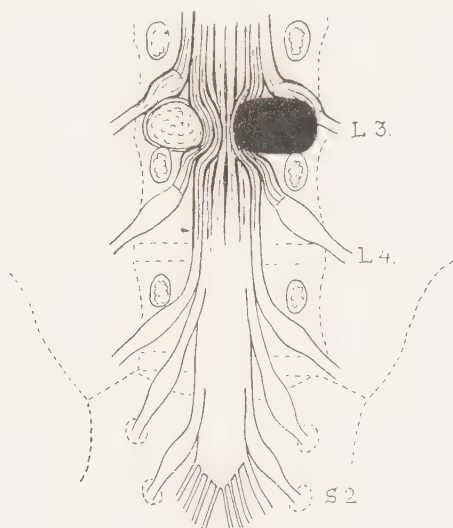


Abb. 2 b.

Kompression von ventral her durch eine sich vergrößernde Discushernia (getüpfelt, links) oder von dorsal her durch vordringendes Gelbband (vollschwarzes Gebiet).

des Gebietes der Zwischenwirbelscheibenpathologie. Es könnte sich hier somit um die erstmalige Prägung eines derartigen Krankheitsbildes handeln, dessen morphologisches Substrat noch darzutun bleibt. Die chronologie: zunächst radikuläre Schmerzen, nachher Kompressionslähmung ist in der Neuropathologie etwas Gewöhnliches, allerdings ist die Frist hier sehr lange bemessen (zehn Jahre).

Es bleibt somit noch die Ursache des klinisch ergründeten spinalen Druck-(Kauda)syndroms darzutun, und die Höhen-diagnose, etwa L. 3 wäre zu präzisieren.

Die Myelographie verbürgt nicht immer die Klärung lumbaler diskusartiger Pathologie. Kleine Hernien werden nur bei grösser Aufmerksamkeit ertappt. Weit lateral befindliche Protrusionen beeinträchtigen den Subarachnoidalraum gar nicht, entgegen der genauesten myelographischen Diagnostik. Röntgenologisch erfasste Hernien können indolent sein. Auch sonst brauchen sie sich bei der Laminektomie in Bauchlage nicht mehr vorzuwölben, sie können dann nur einer federnden Intervertebrallstelle entsprechen. So gelingt es wohl auch einmal eine Diskusprotrusion auf dem Operationstisch mittels interspinösen hebelnden Meiszeinsatzes — im Sinn der Reklination — hervorzurufen.

Im allgemeinen beeinträchtigt eine Zwischenwirbelscheibenläsion den Spinalnerven des nächstunteren Intervertebrallochs, gelegentlich auch des zweitnächsten Foramen intervertebrale. Nur bei weit lateralen Sitz kann der Nerv des eigenen, hinzugehörigen Intervertebrallochs (mit-) geschädigt werden. Die frei im Duralsack liegenden, weiter unten austretenden (lumbo-) sakralen Wurzeln entweichen dem Herniendruck solange nicht besonders grosse vordrängende Nucleusmassen die gesamte Cauda equina komprimieren. Derartige Kaudasyndrome sind immerhin selten. Es ist allerdings zu bedenken dass die Diskussymptomatologie auch durch Hypertrophie eines Ligamentum flavum hervorgerufen werden kann. Dann findet die Nervenkompression von hinten her statt. Auch wurde mehrfach über die Kombination: Nucleushernie und Hypertrophie des gelben Bandes berichtet.

Von der Myelographie könnten verschiedene Ergebnisse erwartet werden, im freien Intervall und während der anästhetischen, schlaffen Parese. Es war allerdings fraglich ob sich bei der gewöhnlichen baskulierenden Untersuchung auf dem annähernd horizontalen Tisch — in der symptomfreien Haltung überhaupt etwas zeigen würde. Es galt somit den Lendenteil der Wirbelsäule in gestreckter Haltung zu myelographieren. Dazu wurde der Patient aufgefordert im Stehen die neuerliche Ausbildung des Kaudasyndroms abzuwarten. Erlaubnis in die Knie zu sinken. Cysternenpunktion und Einverleibung des Lip-

jodols. Erste Aufnahme: des Kontrastmittel hatte die Lumbal-region noch nicht erreicht. Während der Vorbereitung zur zweiten Aufnahme konnte der Patient die ihn quälende Haltung nicht länger aushalten, er stützte sich mit der Brust. Wohl infolge der nicht mehr lordotischen, orthostatischen Wirbelsäule — die Lähmung hatte sich zurückgebildet — war alles Lipjodol zu Boden gesunken. Ein etwaiger Stopp wurde nicht ertappt. Damit war übrigens die Möglichkeit mit der eingespritzten Lipjodoldosis einen etwaigen orthotischen Stopp zu erfassen für immer entwischt.

Es blieb nur noch die Möglichkeit nach Protrusionsaussparungen und dgl. zu fahnden während des üblichen Baskulierens.

In symptomfreier Haltung der Lendenwirbelsäule hat die sorgfältige Myelographie im Gebiete von L. 2/3 die einschliesslich L. 5/S. 1 jedoch nicht Pathologisches aufgedeckt.

Die vorgenommene Laminektomie musste sich also nur auf klinische Daten stützen. Da der dritte Lumbalnerv als kranialster mitbeteiligt war könnte der Diskus L. 2/3 oder das entsprechende Lig. flavum an allem Schuld sein; bei auch weit lateral sich auswirkendem Druck könnte jedoch auch der nächstuntere Diskus, bzw. das entsprechende Gelbe Band die Ursache sein.

Dementsprechend wurde eine Laminektomie von L. 2 (kaudale Hälfte), L. 3 (total) und L. 4 (kraniale Hälfte) ausgeführt. Übliche örtliche Betäubung. Eine Hernia nucleii pulposi wurde nicht gefunden, dafür machte das Lig. Flavum L. 3/4 einen sehr verdickten Eindruck. Der Druck auf dieses Ligament rief erwartetermassen keinen Schmerz hervor — im Syndrom fehlte jeglicher Schmerz. Im Gebiet der angedeuteten Segmente wurde durch ausgiebige Bandexzision dem Duralsack, den Nerven möglichst viel Raum geboten. Die Eröffnung der Dura deckte nichts Besonderes auf, kein Angiom oder dgl. Es blieb somit bei einer Dekompressivlaminektomie.

Der Erfolg war glänzend: der Patient kann seitdem stundenlang gehen, beschwerdefrei, das Kaudasyndrom ist behoben.

An der Konzeption des lordotischen (orthotischen) Kaudasyndroms als Manifestation einer Gelbbandhypertrophie (bzw.

Diskusprotrusion) ist ein Zweifel nicht mehr berechtigt. Und beim eingangs erwähnten unvollständig erforschten Mann es sich um Dasselbe gehandelt haben. Der Mechanismus der Lordosierung als Ursache der Druckerscheinungen seitens eines hypertrophischen Gelbbandes (oder einer Diskusprotrusion) bedarf kaum der Erläuterung: Die Wirbelbogen werden dabei einander genähert, die Gelbbänder verdicken sich. (Diskushernien werden in den Wirbelkanal besonders vorgepresst.)

Dieser Prozess ist meistens nicht sofort, bzw. in absehbarer Zeit reversibel. Wenn auch manche Spinalkompression mit Radikularschmerzen anfängt, so harpte doch die Ablösung des anfänglichen Ischiasbildes mit dem Schmerz als Hauptsymptom durch Jahre später unvermittelt eintretende Lähmung bei meinem Patienten doch einer Erklärung. Ich möchte dieselbe suchen im nunmehr sofortigen Vordringen des verdickten gelben Bandes, derart stark dass ein Wurzelschmerz nicht zur Ausbildung gelangt. Von übergrossen Diskusmassen könnte ich mir dasselbe denken. Die durch die sukzessiven objektiven Untersuchungsbefunde sichergestellte Anästhesie scheint mir in dem Sinn begreiflich, dass die Hypertrophie des gelben Bandes zunächst nur die medial befindlichen nächst- und übernächst unteren Spinalnerven (L. 4, 5) beeinträchtigt. Das stärkere Vordringen komprimiert einerseits den Spinalnerv des eigenen Foramen intervertebrale (L. 3): die Anästhesie übersteigt das Knie; anderseits geraten nunmehr sämtliche sakrale Kaudakurzeln in Druckgefahr: Hypästhesie der Hinterseite, des Perineums und des anschliessenden Gesässes (Sakralnerven, besonders S. 2, 3, 4). Das Radikularsyndrom hat sich unter unseren Augen ergänzt zum gleichfalls ephemeren Kaudasyndrom.

Das Fehlen beweiskräftiger Liquorveränderungen erklärt sich wohl aus der jedesmal nur während weniger Minuten vorhandenen Beschwerden und aus deren vorübergehender Kompressionsursache. Mit dem orthotischen (lordotischen) Kaudasyndrom ist übrigen die folgende Tatsache noch in guter Übereinstimmung: der (2.) Patient hatte keine Beschwerden beim Tennisspiel. Dabei steht man nämlich nicht mit gestrecktem Rücken sondern vorn herüber gebeugt.

Die groben Gehstörungen gehören nicht zum typischen Ischiasbild der durchschnittlichen Diskusvorwölbung oder Gelbbandhypertrophie mässigen Umfangs. Die Beeinträchtigung besonders der Nerven L. 4, 5 verursacht nur eine leichte allgemeine Parese und eine nur an unilateralen Fällen feststellbare konsequente Atrophie. Das ataktisch-paretische Gepräge des Ganges dagegen ist bei einem Kaudasyndrom verständlich.

Den vermuteten lordotisch-orthotischen Stopp als Block auf dem Wege der kombinierten Funktion zu erhärten schien ausichtslos in der nur in Betracht kommenden Haltung, die es nicht gestatten würde die Schwerkraft auszuschalten.

Der negative Lasègue wundert mich nicht sosehr. Die diesbezügliche Prüfung setzt entweder die entlastende Rückenlage voraus oder — im Stehen — die Rückenkrümmung im kyphotischen Sinn. Ein lordotischer Prozess dürfte somit den Lasègue praktisch ausschliessen: es dürfte auch sein Fehlen bei mancher gewöhnlichen Diskus-ischias erklären indem die daraufhin zielende Untersuchung zwar den Nerven streckt, entspannt aber auch die verdickte Gelbbandmasse streckt — bzw. die Diskushernie mehr oder weniger reponiert. Mancher diskogene Ischias scheint nämlich gleichfalls orthotisch-lordotisch betont, es fehlt allerdings in gewöhnlichen Fällen die prompte, dramatische Reversibilität.

Die beiden beschriebenen Fälle dieses Beitrags haben sich dargeboten in einer Reihe von mehreren Dutzenden Patienten, die wegen gewöhnlicher radikulärer Diskus (Gelbband)-symptomatologie erfolgreich operiert wurden.

ZUSAMMENFASSUNG

Beschreibung zweier Patienten mit einem reversibelen, orthotisch-lordotischen Kaudasyndrom. In den einen, auch erfolgreich laminektomierten Kranken stellte sich eine Hypertrophie des Gelbbandes als Ursache heraus. Anästhetische und ataktisch-paretische Symptomatologie, als deren Ursache sich künftig auch einmal eine massale Diskusprotrusion manifestieren könnte.

Eine sonstige Verengung des Spinalkanals — auch etwa eine Paget'sche Knochenerkrankung — hat nicht vorgelegen.

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PATHOGENESIS OF CRANIAL NERVE LESIONS, NOTABLY OPHTHALMOPLEGIAS, COMPLICATING HERPES ZOSTER OPHTHALMICUS¹

BY

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It is well known that herpes zoster ophthalmicus is sometimes—though rarely, indeed—complicated by other cranial nerve lesions, most often ophthalmoplegias. The pathogenesis, however, being still obscure the subject will be discussed here on the basis of the writer's own observations.

The incidence of herpes zoster ophthalmicus with and without attending ophthalmoplegia will be briefly mentioned. Though several cases of herpes zoster ophthalmicus are submitted to out patient treatment, those admitted to an Ophthalmological Department (where they constitute 1 per cent) are no doubt in the majority. 100 such cases were observed in the Ophthalmological Department of the *Kommunehospital* within the past decade (1937-47). Only a small number (3 cases in all) presented ophthalmoplegia as well. This incidence corresponds to that observed by *P. Ehlers*, who among 20 cases of herpes zoster ophthalmicus collected from the *Blegdamshospital* over a 9-year period found only one with sixth and seventh nerve paralyses (homolateral). From America (*Donahue*) we have statements of a higher incidence: 7 to 24 per cent.

The literature on concurrent ophthalmoplegia and herpes zoster is chiefly casuistic with Scandinavian contributions by

¹ Read before the Oto-Neuro-Ophthalmological Society on May 7, 1947.

Dalsgaard-Nielsen (1935) and *Essen-Möller* (1936), of which further mention will be made below.

The symptomatology of herpes zoster ophthalmicus associated with ophthalmoplegia will be briefly stated on the basis of the writer's own observations and cases published recently in the literature.

Case 1. (Ophth. Dept., K. H. 547/45). A man, aged 63, suffering from chronic primary progressive polyarthritis, bronchial asthma, and chronic bronchitis (of 3 years' duration) developed croupous pneumonia, responding favourably to sulphathiazol treatment. 8 days after the onset of pneumonia the patient developed a typical left herpes zoster along the course of the ophthalmic nerve, which became complicated by keratitis, and later with glaucomatous iridocyclitis. 3 weeks after the herpetic eruption there occurred a left total sixth nerve paralysis, which persisted unchanged for 3 months, then to disappear entirely again. Cerebrospinal fluid examination at the onset of the herpes showed as follows: 6/3 cells, 75 albumin, 9 globulin (a.m. *Bisgaard*). Wassermann-reaction negative.

Case 2. (Physician-in-Chief H. U. Møller's consultation). An otherwise healthy man, aged 67, developed without any preceding febrile disease, a left typical herpes zoster along the course of the ophthalmic nerve with no affection of cornea or iris, but with hypaesthesia in the ophthalmic nerve area. 8 days later there occurred a left total third nerve paralysis persisting unchanged for 2 months, after which it gradually improved. No examination of the cerebrospinal fluid, because the patient refused to be sent to hospital.

These two cases have been entered in Table 1 together with four similar cases published by *Dalsgaard-Nielsen*, *Essen-Möller*, *Parry & Laszlo*, and *Donahue*. In 5 of the 6 cases the herpes was localized along the course of the ophthalmic nerve. The sixth case, with localization in the thorax (*Parry & Laszlo*), was included on account of the ophthalmoplegia. To the data indicated in the Table may be added the facts that preceding febrile disease was found only in the writer's observation No. 1, and that no cases of chicken-pox were found in the patients' immediate surroundings.

The ophthalmoplegia developed after the herpetic eruption in all 6 cases (from 1 to 8 weeks; most often 3 weeks or less: 4 cases). The ophthalmoplegias were solitary in 5 cases, due to

TABLE 1

Six cases of herpes zoster complicated with ophthalmoplegias.

Author	Sex Age	Localisation of zoster	Ophthalmoplegia			Cerebrospinal fluid		
			Onset in week after zoster- eruption	Nature	Dura- tion (mth)	Cells 1/3	Alb.	Glob.
Dalsgaard-Niel- sen 1935	F 76	left ophthalmic	2	III	1½	36	13	0—1
Essen-Möller 1936	M 22	do.	3	III	6	17	+	+
Parry & Laszlo 1943	M 33	Thorax	3	VI	?	slight increas.	+	+
Donahue 1946	F 54	ophthalmic	8	III, IV, VI	2	?	?	?
Own case 1	M 63	left ophthalmic	4	VI	3	6	75	9
Own case 2	M 67	do.	1	III	>2	?	?	?

lesion of the third cranial nerve in 3 cases and of the sixth in 2 cases, while only one case (*Donahue*) presented total external ophthalmoplegia. All the paralyses were ipsilateral to the zoster. The patients recovered completely from the ophthalmoplegia after 2 to 4 months. Examinations of the cerebrospinal fluid, undertaken in 4 cases, revealed slight pleocytosis (6/3-33/3 cells) and slight (in the writer's obs. No. 1 considerable) hyperalbuminosis.

No further comments will be made on the herpes zoster as such, which ran the usual course. Of interest from an ophthalmological point of view is the fact that 4 cases were complicated by iridocyclitis, partly with (*Essen-Möller*, *Donahue*) and partly without (*Dalsgaard-Nielsen*, the writer's obs. No. 1) attending increase in the intraocular tension.

The above 6 cases of concurrent ophthalmoplegia and herpes zoster are representative with regard to the nature of the ophthalmoplegias as indicated in the current text-books (*Willbrand*

& Saenger, Kinnier Wilson, Bumke & Foerster), according to which paralysis of the seventh cranial nerve should be a still more frequent complication.

Facial paralysis in connexion with herpes zoster ophthalmicus (without ophthalmoplegia) was observed in the following case (Ophth. Dep. of the *Rigshospital*, Case 75/47):

A woman, aged 57, who 2 months previously had had herpes zoster of the thorax (left), was now admitted with herpes zoster along the course of the ophthalmic nerve with corneal eruption, but not iritis. Well over one week after the appearance of the herpetic eruption there occurred a right peripheral facial paralysis, which subsided almost completely in the course of five or six weeks. Otological examination revealed a normal tympanic membrane and right impairment of hearing of the perception type (auditory nerve lesion?). Examination of cerebrospinal fluid: Pleocytosis (65/3 cells) and slight hyperalbuminosis (17 albumin, 0 globulin). A control examination one month later showed remission (44/3 cells and normal albumin values).

Herpes zoster ophthalmicus may be complicated by other cranial nerve lesions, but these will be left out of account in the present paper, except for the optic nerve lesion, which will be mentioned in the discussion on the pathogenesis. A case of this rare complication of *herpes zoster ophthalmicus and optic neuritis* will therefore be reported here (Ophth. Dept. K. H. 417, 46)¹:

A previously healthy man, aged 65, without any preceding febrile disease, developed a left herpes zoster along the course of the ophthalmic nerve. 12 days later there was observed a massive, left visual impairment (vision 6/60) with a large central scotoma extending into the upper half of the visual field. There was no keratitis, iritis, nor ophthalmoplegia. The retrobulbar neuritis persisted unchanged through two months of observation with a considerable visual field defect (only lower nasal quadrant preserved) and temporal discolouring of the disk.

A similar case reported by *E. Holm* (1941), where the visual impairment persisted only for ab. 10 days, shows that retrobulbar optic neuritis may subside within a short time.

¹ This case was the only one of optic nerve lesion among the 30 cases of zoster observed since 1944.

DISCUSSION

The above cases of herpes zoster ophthalmicus associated with other cranial nerve lesions are illustrative of the different pathological pictures. The cause of the occasional complication by other neurological signs and symptoms has not been evidenced so far. The cutaneous extension, severity, duration, etc., of the herpes do not differ from what is seen in other cases without attending neurological symptoms, and the prognosis is almost the same, even for cases with changes in the cerebrospinal fluid. The prognosis was best for the lesions of the motor nerves (complete recovery), while it was severer for the optic nerve lesion. The visual impairment was here permanent, or at least of long duration, in contrast with the course of other retrobulbar neuritis, which generally subside within 2 to 5 weeks.

The pathogenesis of the cranial nerve lesions complicating herpes zoster ophthalmicus is in the neurological text-books (*Bunke & Foerster*, *Kinnier Wilson*, and *Purves Stewart*) and by *Dalsgaard-Nielsen*, *Essen-Möller*, *Parry & Laszlo*, and *Dona-hue* indicated as a radiculomeningitis proceeding from the part of the gasserian ganglion in which the herpes zoster virus is localized, and where pathologico-anatomical examinations (*Head & Campbell*) have revealed a very pronounced haemorrhagic inflammatory reaction in the ganglion cells, with necrobiosis, necrosis, and consecutive regional meningitis. Despite the often vehement course of the inflammation in the ganglion it is generally limited to the first trigeminal area, as in the present cases. Among *P. Ehlers'* 20 cases there was one with transition from the first to the second trigeminal area. The inflammation spreads both centrifugally and centripetally from the ganglion along the trigeminal fibres (*Head & Campbell*). The progression of the inflammation towards the cavernous sinus and the eye nerves running here (Fig. 1) explains the affection of these nerve stems as well as the order of frequency of the affection (III, VI, and most rarely IV nerve).

The possibility can hardly be excluded that the facial paralysis sometimes complicating herpes zoster ophthalmicus may like-

wise be explained as a consequence of radiculomeningitis proceeding from the gasserian ganglion. Yet the far greater distance from the gasserian ganglion to the facial nerve than to the eye nerves seems to go against this theory. Since the zoster virus spreads also centripetally into the brain stem (eliciting brain

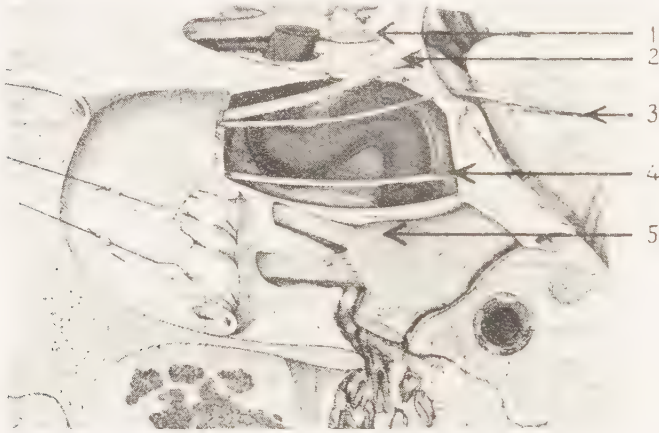


Fig. 1.

Left middle cranial fossa with the cavernous sinus open, seen from the side (after Testut), presenting the optic chiasm and nerve (1), the third nerve (2), the thin fourth nerve (3), the sixth nerve (4) and below the Gasserian ganglion (5).

stem encephalitis) and the most intimate relation between trigeminal fibres (the trigeminal root descending from the mesencephalon) and facial fibres (running from the facial nerve nucleus just medially to the trigeminal fibres) is found in the brain stem (Fig. 2), a brain stem encephalitis gives a more likely explanation to concurrent fifth and seventh nerve lesions. It should be borne in mind that a possible, simultaneously occurring sixth nerve paralysis (as in one of *P. Ehlers'* cases) may likewise be due to a pontine lesion.

Brain stem encephalitis is not mentioned in current neurological and ophthalmological text-books (*Duke-Elder*) as a pathogenetic explanation of cranial nerve lesions in connection with herpes zoster ophthalmicus. In *Alpers'* neurology (1946), on the

other hand, it is stated that 5.7 per cent of the herpes zoster ophthalmicus cases are complicated by encephalitis, localized not only in the brain stem (notably the mesencephalon), but also in other parts of the brain. The symptomatology is varied, comprising ophthalmoplegia, *Argyll Robertson's* symptom, cerebellar

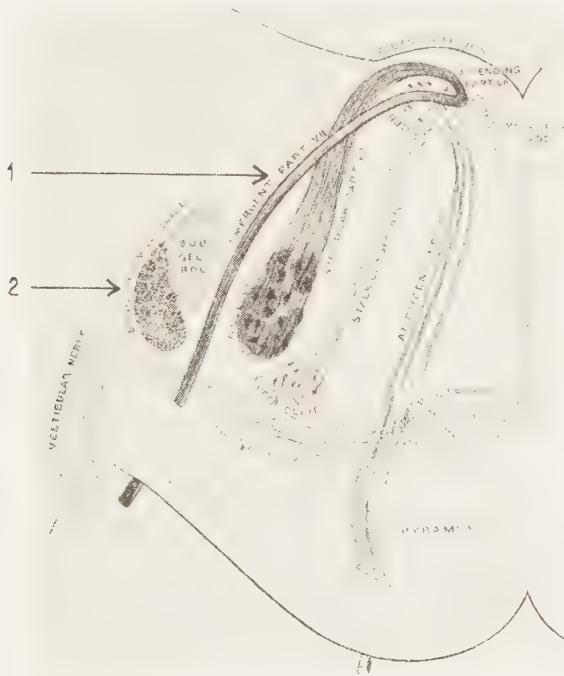


Fig. 2.

Schematic drawing of a horizontal section through the pons (after Cunningham) presenting the intimate relation between the intrapontine part of the facial nerve (1) and the spinal trigeminal tract (2).

disturbances, hemiplegia, and, at a special hemisphere localisation, psychoses, spasms, and coma. The occurrence of radiculomeningitis is not mentioned by *Alpers*.

However, there are various facts going against *Alpers'* somewhat one-sided encephalitis pathogenesis. A topically well-defined pathological picture as retrobulbar optic neuritis can

be explained only as part of a radiculomeningitis. Moreover, if the ophthalmoplegias were due exclusively to a brain stem encephalitis, it is difficult to explain why the lesion of the trochlear nerve is so rare, and why the eye nerves are so frequently affected. A brain stem encephalitis comprising homolateral oculomotor and trochlear nerve nuclei should cause contralateral trochlear paralysis. This has not been observed.

The changes in the cerebrospinal fluid neither support nor go against the possibilities suggested.

It appears from the above discussion that the pathogenesis of cranial nerve lesions in connection with herpes zoster ophthalmicus is hardly *either* radiculomeningitis *or* encephalitis, but rather *both—and*. The conditions are often complex, and encephalitis should be suspected to a greater extent than previously in cases of symptoms originating from the distal cranial nerves (VII, etc.), while radiculomeningitis should be suspected when the symptoms come from the proximal cranial nerves (II, III, IV, and VI).

That the herpes zoster virus may also cause encephalitis corresponds to what has been observed in other virus diseases (measles, mumps, and poliomyelitis). The fact that benign lymphogranulomatosis (*Bocck-Schaumann*), the aetiology of which is unknown, may be complicated by cranial nerve lesions and iridocyclitis (*Godtfredsen*), exactly like herpes zoster ophthalmicus, argues in favour of the theory of a virus as the aetiological factor in the case of *Bocck-Schaumann's* disease.

CONCLUSION AND SUMMARY

8 cases are reported of herpes zoster ophthalmicus complicated by cranial nerve lesions. The pathogenesis of these lesions is discussed and supposed to be a radiculomeningitis in the cavernous sinus region in the case of the eye nerves (II, III, IV, and VI), while facial paralysis and other bulbopontine symptoms are supposed to be due to brain stem encephalitis.

Even though complication by other cranial nerve lesions does not tend to worsen the prognosis these cases no doubt

require longer confinement to bed, and they must be regarded as particularly suited for treatment with the convalescent serum now available.

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ENCEPHALOGRAPHIC INVESTIGATIONS OF PSYCHIATRIC PATIENTS

BY

ARNE HAUGEN AND JOHAN HOVE

In order to get an impression as to the utility of encephalographic examinations of psychiatric patients we have gone through the encephalograms taken from patients in the Psychiatric Department of Ullevaal Hospital during the years 1941-1944. During these four years in all 314 encephalograms from altogether 259 patients have been recorded. In the same period 3897 patients were admitted to the department (including all admissions, not only patients admitted for the first time). Thus encephalography has been performed on about 6.6 per cent. of the total number of admissions.

Similar investigations had previously been carried out, for instance in Psychoneuroses (*Wigert 1938*), Neuroses and Disorders of a Neurotic Character (*Bredmose and Munch-Petersen 1940*), Epilepsy (*Dickerson 1941*), Presenile Dementia (*Romano and Miller 1940*) and in Psychoses (*O. Schiersmann 1943*).

The selection of patients for encephalography was mainly dictated by clinical-therapeutic considerations, the encephalograms being taken in cases where the result of this form of examination might be supposed to be of significance for the diagnosis and treatment.

Encephalography was not carried out in all cases where positive findings might be expected, for example, not where there was otherwise sufficient data for the judgment of the case. Thus, encephalography was not usually employed in the case

of paralytics or in undoubtable cases of senile dementia—even if these patients presented symptoms which are otherwise regarded as indications for such examination.

Naturally, the procedure was likewise refrained from in cases where it might be expected to involve serious danger, such as expansive intracranial processes with signs of increased cerebral pressure (choked disks, cranial alterations).

With the reservations mentioned, encephalography was carried out on all patients with epileptic manifestations, as well as on patients with obscure disorders, where either the psychiatric picture or somatic findings might point to organic disease of the brain.

The scrutinizing of the radiograms was done by different examiners during the four years which the investigation embraces. We have re-examined the pictures and have found good concordance between our results and those arrived at by previous investigators. Of the 314 encephalographies 276 were ordinary (subarachnoidal) insufflations, while in 38 cases the object was that of examining the subdural space. The two forms of examination are in so far different that it has been found most convenient to deal with them separately.

Ordinary encephalography was in 184 cases effected by the combined cisterno-lumbar method, in 88 cases by the lumbar method and in 4 cases by cisternopuncture alone.

In all encephalographies air was used for the insufflation, which was performed in the psychiatric department, with the patient in a sitting posture, and the patients were then conveyed on stretchers to the roentgen department. Thus no insufflations were made during fluoroscopy. It was endeavoured to adapt the quantity of air according to the nature of the particular case (small quantity of air where there was a possibility of cerebral tumour, larger quantity where cerebral atrophy was suspected).

The combined cisterno-lumbar encephalographies are effected by a modified method devised by Dr. *Ole B. Munch* (personal communication):

The patient is placed on a special chair (modification of the Antoni model) with a head-rest.

Cisternal and lumbar puncture: Both needles are connected by rubber tubes with an apparatus, the principle of which is as follows: The fluid from the lumbar needle drops out into a closed receptacle. The air expelled from the receptacle passes through a closed system into the cistern needle. Superfluous air can be taken up by a Record syringe connected with the system. Before the cistern needle is inserted a receiver containing sterile hot water, about 4 cc. high. Here the passage of the air can be noted by the naked eye. The cistern needle is likewise in uninterrupted connection with a water manometer, off which the pulsatory variation in pressure can be read, which is a good indicator of the correctness of the insufflation procedure. During the insufflation it is endeavoured to regulate the quantity of air and the rapidity of outflow, so that the initial pressure in the cistern (usually about ± 0) is maintained. The insufflation may take place relatively quickly, about 10 cc. per minute, without increased discomfort to the patient.

For subdural encephalography the same apparatus is employed, with use of a method described by Antoni (l. c.).

With open recipient, a sufficient quantity of lumbar fluid is first tapped out, usually about 25 cc., to cause the lumbar pressure to fall about 100-200 mm. (The patient then reports a bursting sensation in the head). The cistern needle, with short point and lateral aperture, fitted to the manometer of the apparatus, is cautiously introduced without use of a mandrin. As soon as it has passed through the dura, a great reduction of pressure will be noted. Through the firmly attached Record syringe air is now introduced in order to counterbalance the reduced pressure. Thereupon the replacing of fluid by air is continued until about 50 cc. of air have been introduced. Half of the air is passed in with the head bent over to the left, the other half with the head bent over to the right.

The lumbar insufflations were effected in the simplest manner, the air being injected by aid of a Record syringe directly attached to the puncture-needle. As was formerly usual, the quantity of air injected was a little smaller than the quantity of fluid removed.

After encephalography the patients were kept in bed until the post-encephalographic discomforts subsided, or for at least two days. The patients lay with the head kept low, and in cases of marked distress medicaments were given.

In the cases where cisternal puncture alone was performed there was a free inflow of air. The exact quantity of air admitted in these cases therefore is unknown. Otherwise the quantity varied between 10 and 140 cc. On an average for all the ordinary encephalographies the amount of air injected was 36.58 cc.

The 276 ordinary encephalographies were carried out on 230 patients, each patient having been encephalographed from 1 to 4 times. The age varied from 9 to 70 years, the average age being 38.53 years. There were 110 males of an average age of 38.07 years and 120 females of an average age of 38.95 years.

The investigations have been divided into the following groups, according to the results:

- (1) "Complete investigations", which embrace the positive and negative findings and which illustrate the usefulness of the method.
- (2) Doubtful findings, which may have been of some value.
- (3) "Incomplete investigations", indicative of a failure of the method.

Of the 276 encephalographies we have:

171 complete (39 pos. and 132 neg.),	<i>i.e.</i> about 62 per cent.
48 doubtful,	<i>i.e.</i> over 17 per cent.
57 incomplete,	<i>i.e.</i> about 20½ per cent.

Positive findings were made in 39 encephalographies, *i.e.*, in over 14 per cent. (of 276).

The positive findings were made in 34 patients (out of 230) also over 14 per cent.

The nature of the 39 positive findings was:

Hydrocephalus int.	22 (19 patients).
Expansive processes	7.
Porencephalia	5 (4 patients).
Cerebral atrophy	5 (4 patients).

The 48 doubtful findings were:

Hydrocephalus int.	6.
Cerebral atrophy	17.
Shrinkage of one hemisphere	1.
Ventricular asymmetry	8.
Septum pellucidum cyst	3 (1 patient).
Low-lying anterior horn	2.
Absence of septum pellucidum	1.
Prominent choroid plexus	1.

Altogether 39 doubtfully positive findings and 9 cases in which the diagnosis probably was negative findings, but where the insufflation was too imperfect to permit of absolutely certain diagnosis.

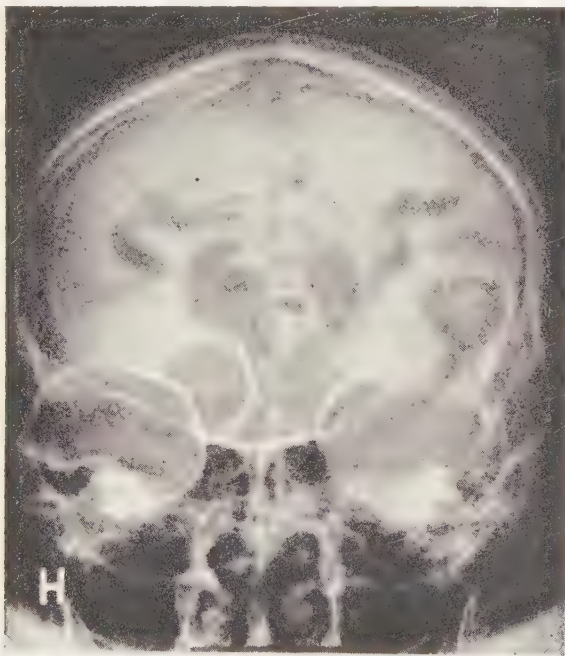


Fig. 1.

Woman aged 63. Cerebral atrophy. Slightly expanded ventricular system.
Dilated sulci on the convexity.

The group of doubtful findings thus consists partly of cases in which the radiological findings have in themselves been uncertain and partly of cases where the findings undoubtedly deviate from the normal, but where it could not be said with certainty whether the anomaly was of any pathological signi-

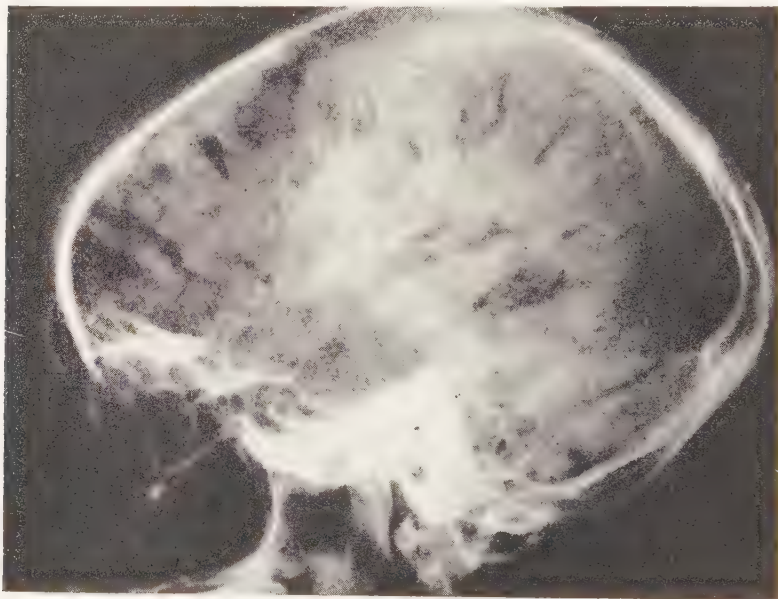


Fig. 2.

Woman aged 48. Uncertain cerebral atrophy.
Some dilation of sulci on the convexity (no expansion of the ventricular system).

ficance or not. It will be noted that there are only 5 certain cases of cerebral atrophy, but 17 uncertain. Doubtless an indication of caution in the judgment of these conditions.

In the following table is given a synopsis of the chief diagnoses for the encephalographed patients and of the findings made.

However, this synopsis does not for all the groups of diseases give an adequate expression of the indications for encephalo-

Diagnosis	♂ ♀		X-ray findings			Doubtful	No. of pat.	No. of examin.	Positive findings	Doubtful pos. findings
			pos.	neg.	0					
Neurosis	10	22	21	10	6	32	37	Cerebral atrophy 1 Hydrocephalus 1 Ventric. asymmetry 2		
Psychopathia	9	9	3	12	1	18	19	Cerebral atrophy 2 Hydrocephalus 1		
Oligophrenia et psychosis ex imbecil.	7	17	7	12	5	24	36	Hydrocephalus int. 7	Low anterior horn 1 Cerebral atrophy 2 Ventric. asymmetry 3 Sept. pelluc. cyst 3	
Psychosis gen. incert.	6	6	6	6	6	6	6			
Vit. organ. cerebri et psychosis ex vit. cerebri	12	11	10	7	3	23	29	Hydrocephalus int. 7 Cerebr. atrophy 2 Porencephalia 1	Cerebral atrophy 6 Hydroceph. int. 1 Promin. plex. chor. 1 Ventr. asymmetry 1	
Psychosis luogenes	2	3	2	1	2	5	5	Cerebral atrophy 2		
Alcohol.chr. et narcomania	13	3	5	10	2	16	19	Hydrocephalus int. 1 Porencephalia 3 Expans. proc. (subdur. hem.) 1	Cerebral atrophy 2	

Synopsis (cont.)

Diagnosis	X-ray findings				Doubtful	No. of pat.	No. of examin.	Positive findings	Doubtful pos. findings
	♂	♀	pos.	neg.					
Psychosis ex const.	4	3	4			7	8		
Endogenous psychoses, (Schizophrenia & man- mel. psychosis	1	2	1	1	1	3	3		Low anterior horn 1
Psychosis ex involutione et senio	2	7	4	3	1	4	9	12	Cerebr. atrophy 3 Hydrocephalus int. 1
Expansive intracranial processes	3	4	6		3		7	9	Expansive process 6
Sequelae traum. cap.	14	7	17	5	2		21	24	Hydrocephalus 1
Epilepsia et psychosis epilep.	27	22	4	32	17	6	49	59	Cerebr. atrophy 1 Hydroceph. int. 1 Ventr. asymmetry 2 Shrinkage of one hemisph. 1 Absence of sept. pellucid. 1
Other fairly rare diagnoses	6	4	5	4	1	10	10		Hydroceph. int. 1

graphy. For example, the reason for encephalography in case of an alcoholic has seldom been the alcoholism itself, but far more frequently an injury to the head. As might be expected, most of the positive findings were noted in diseases of an undoubtedly organic nature. Positive or doubtfully positive findings, however, have also been made in some groups of diseases where one perhaps would hardly have expected them. We shall not attempt to enter into any detailed discussion of this matter, but we may mention that in our material there has always existed one or more special reasons for the adoption of encephalography (antecedent encephalitis, head-injuries, etc.). It will be seen that 50 patients suffering from neurosis or psychopathy were subjected to encephalographic examination. Meanwhile, the total number of patients treated for these disorders in the department during the same period was 963.

In this connection Professor *Wigert's* discourse at the Psychiatric Congress in Oslo in 1938 may be mentioned, where he stated that positive encephalographic findings are not infrequent in the conditions designated Psychopathies and Psychoneuroses (*Wigert* 1938).

We have gone through the case-records in order to find the special reasons for the employment of encephalography, and it is seen that some particular factors have predominated in such cases. Epilepsy and epileptiform manifestations were present in 102 cases (out of 230), that is to say, in over 44 per cent.

Head-injuries are mentioned in the anamnesis in 85 cases, or about 37 per cent.

These figures, however, cannot be added up, since many of the patients with epilepsy or epileptiform manifestations were also suffering from injuries to the head.

Other reasons for the adoption of encephalography have been persistent headache, endocrine derangements, neurological findings, etc., which were suggestive of organic brain disease. In some cases there were several indefinite features which, taken together, rendered an encephalographic examination desirable. Therefore, we have not cited figures for the different indications, apart from the above-mentioned predominant reasons.

In conclusion, we shall mention the defects of the method. Apart from the fact that the encephalographic examination in some cases fails to provide serviceable information (over 20 per cent. of the examinations were incomplete and more than 17 per cent. gave uncertain results), it entails some distress for the patient, and we must reckon with the possibility that it may be dangerous.

Two of the patients in our material died about five days after encephalography had been performed. One of these patients had a malignant glioma and the other a cystic tumour at the bottom of the third ventricle, with a massive and progressive diencephalic syndrome. Both patients would certainly under any circumstances have succumbed in the course of a short time. As to whether the death was to any degree hastened by the encephalography nothing can be said with certainty, but the cases must be taken as a reminder that the greatest caution must be exercised in dealing with cerebral tumours.

During the process of insufflation three of the patients fainted and in two cases epileptic attacks supervened (in epileptics). All five patients rapidly recovered.

In 56 cases the patients suffered no particular discomfort during the insufflation. In the remaining cases there was more or less distress of the usual kind, with headache, pallor, sweating or tendency to vomit. Of troubles arising after encephalography we have especially noted headache, vomiting, dizziness and rise of temperature. (A record has been kept for each patient during six days.)

Duration of headache

Days:	0.	1,	2,	3,	4,	5,	6,	Uncertain
								number.
Encephalographies:	57,	45,	44,	29,	24,	22,	52,	3.

Headache has thus occurred in over 79 per cent. of the cases and the average duration has been 2.70 days per encephalography. Many of the patients had had headache in the anamnesis and, since in some such cases it must be deemed difficult to decide whether the headache occurring after the encephalography was

really due thereto, we have also calculated the average duration of the headache in the patients who had not had any mention of headache in the anamnesis. On these patients 168 encephalographies were performed and they had headache with an average duration of 2.45 days after the examination. The quantity of air injected was about equally large for the two groups of patients, namely, on an average respectively 36.58, and 35.47 cc.

Comparatively many of the patients had a headache for six days, and it must naturally be expected that in some of these cases the headache in reality lasted longer, but the records after the first six days are not sufficiently exact to be taken into account. The figures found for the average duration of headache must therefore be regarded as somewhat too low.

Days of *Vomiting*: 0, 1, 2, 3, 4, 5, 6, uncertain number.

Encephalographies: 200, 60, 9, 4, 1, 1, 1.

Vomiting occurred in about 27½ per cent. of the encephalographies, most often in immediate conjunction with the insufflation.

Days of *Vertigo*: 0, 1, 2, 3, 4, 5, 6, uncertain number.

Encephalographies: 218, 26, 16, 4, 4, 3, 3, 2.

Vertigo was thus present in about 20½ per cent. of the encephalographies.

Rise of temperature to 38° C. or more:

Days: 0, 1, 2, 3, 4, 5, 6.

Encephalographies: 172, 94, 7, 2, 1.

Rise of temperature, which occurred in about 37.66 per cent. of the cases, most often came to a little over 38° C, and a temperature of 39° or more was noted only in 5 instances. (One patient showed a rise to 41.9°, but was without fever after two days.) In some cases the rise in temperature was of so short duration that it was revealed only by hourly measurements.

In *Guttmann's* chapter on diagnostic radiography of the brain and spinal cord in the *Handbuch der Neurologie* (1936) it is stated that rise of temperature is a regular consequence of encephalography.

In order to form an idea as to how far the duration of the predominant symptom, namely headache, is dependent on the quantity of air injected we have drawn up a table showing the quantities of air in groups and the corresponding duration of headache in days:

Quantity of air, in cc.	10-20	21-30	31-60	Over 60
Average duration of headache, in days	2.38	2.57	2.82	3.35

There is here seen a rise in the duration of the headache in accordance with increasing injection of air.

As regards the other deleterious effects of encephalography, the figures are too small to admit of division into groups. It should merely be mentioned that in 130 cases up to 30 cc. of air was injected and that a rise in temperature was noted in 40 of these cases, or nearly 31 per cent., while in 141 cases the quantity of air injected was over 30 cc. Here there was a rise of temperature in 61 cases, *i.e.* fully 43 per cent. As the unpleasant effects seem to increase with increasing injection of air, it will be of importance to obtain an idea as to the diagnostic results attained by injection of large quantities of air as compared with small quantities. We have therefore calculated the percentage of complete investigations effected in different groups of encephalographies, arranged according to the quantity of air injected:

Quantity of air, in cc.	10-20	21-30	31-60	Over 60.
Complete investigations	60.40 %	64.63 %	62.18 %	65 %.

From this table it seems as if the number of complete investigations does not rise when the quantity of air injected is larger than 30 cc. The number of encephalographies in the different groups, however, is not particularly large and therefore no definite conclusions can be drawn. It is quite probable that 30 cc. in most cases is too small a quantity for an effective judgment of both the ventricular system and the subarachnoidal space over the convexity. *Davidoff* and *Dyke* (1946) suggest 50-70 cc. and *Busch* (1945) for the traumatic lesions recommends

60-70 cc. For examination of the ventricular system alone it is, however, possible that small quantities of air may be sufficient in most cases. *Davidloff* and *Dyke* remark that if the air has not got into the ventricular system after the injection of 20 cc., it will seldom do so on further injection.

Finally, it is to be mentioned that the material here dealt with is not serviceable for the discussion of possible advantages and defects in the different methods of insufflation, seeing that most of the minor encephalographies were effected by the lumbar method and the more extensive operations by the cisterno-lumbar method, while injection by cisternal puncture alone was adopted only in some few cases and then with free ingress of air.

The average quantity of air injected by the cisterno-lumbar method was 42.25 cc. and by the lumbar method 24.80 cc.

SUBDURAL ENCEPHALOGRAPHIES

In addition to the ordinary encephalographies attempts at subdural injection of air were made in 38 cases during the four-year period under consideration. These 38 examinations were carried out on 29 patients, 25 men and 4 women. (Some of them were also examined by ordinary encephalography.)

All the subdural injections were effected by the methods previously described.

The average quantity of air injected was 51.10 cc.

The results were as follows:

- 2 positive (adhesions).
- 14 negative.
- 21 incomplete.
- 1 doubtful (adhesion).

Thus we have complete results (pos. + neg.) in over 42 per cent. and incomplete results in over 55 per cent. of the cases.

Head-injury was reported in the anamnesis in 32 of the 38 cases of subdural encephalography and epilepsy in 16.

The troubles arising in the subdural encephalographies seem

to have been about the same as in the ordinary forms. Headache occurred in 28 cases and the average duration. Calculated for all 38 cases examined, was 2.82 days.

In some cases encephalography was employed both for diagnostic and therapeutic purposes, but these cases were so few that the material has not been considered suitable for investigation of possible therapeutic effects.

If any conclusion were to be drawn from the impression obtained, it must be that encephalography—even though the positive findings are not very many—is a valuable, and in certain cases indispensable, aid in the examination of psychiatric patients. The risks should not be great, if caution is observed, especially in cases of tumours.

SUMMARY

In Oslo Municipal Hospital, Ullevaal, Psychiatric Department, 314 encephalographies were carried out during the years 1941-1944. Of these cases 276 were ordinary and 38 subdural encephalographies.

Positive findings were made in over 14 per cent. of the ordinary encephalographies. "Complete investigations" (positive + negative findings) together represented about 62 per cent. The method failed entirely in about 20½ per cent. of the cases, and in over 17 per cent. the findings were doubtful. The positive findings were: Hydrocephalus int., expansive processes, porencephalia, and cerebral atrophy. The doubtful findings included comparatively many cases of cerebral atrophy.

A tabular survey shows the relation between the positive findings (certain and doubtful) and the clinical diagnoses.

The most frequently arising reasons for the employment of encephalography were injuries to the head, epilepsy, and epileptiform manifestations.

Two patients (with cerebral tumour) died about five days after encephalography, without it being possible to decide with certainty whether the examination had any influence as regards the fatal issue.

The most commonly arising trouble after encephalography was headache, which occurred in over 79 per cent. of the cases, and had an average duration of 2.70 days.

Rise of temperature (to 38° C. or more) occurred in about $37\frac{2}{3}$ per cent. of the cases, vomiting in about $27\frac{1}{2}$ per cent. and vertigo in about $20\frac{1}{2}$ per cent.

The ill-effects increased on injection of increased quantities of air.

In the subdural encephalographies the "complete results" (positive + negative) represented over 42 per cent.

Two certain adhesions and one doubtful were found.

The troubles arising after the subdural encephalographies were about the same as after the ordinary forms.

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CHRONIC MENINGITIS

BY

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The so-called benign aseptic meningitis has been the subject of continuous interest ever since *Widal* in 1916 and *Wallgren* in 1923 separated it out as a distinct group of symptoms. The question has been discussed in Finland by *Björk* in 1936. In the very extensive literature on the subject little attention has been paid to the chronic symptoms of meningitis.

In order to elucidate the matter in hand it is advisable to take a general survey of the different groups of meningitis. We distinguish three groups of them: (1) the luetic, (2) the purulent, (3) the non-bacterial or aseptic meningitis. The first two will not be discussed here.

Lange distinguishes the following forms of non-bacterial meningitis:

- (1) meningitis sympatica (concomitans)
- (2) benign aseptic meningitis
- (3) meningeal reactions in the parotitis
- (4) meningeal irritations in acute infections and poisonings
- (5) the so-called serous meningitis. *Arachnitis adhaesiva circumscripta et cystica*.

The meningitis sympatica-group presents no etiologically uniform picture. According to *Lange* it is "an inflammatory, non-bacterial reaction of the meninges", caused by bacterial inflammations in the neighbourhood of the meninges. He includes in these the sclerosis multiplex and other non-bacterial cerebral inflammations, cerebral abscesses and the poliomyelitis.

Roeder and *Rehm* hold a different view, according to which the meningitis in question is caused by purulent inflammations and tumours.

The position of the three following groups of *Lange* is more unstable. *Pette* gives the following division with regard to them:

- (1) primary virus meningitis
 - (a) idiopathic aseptic meningitis.
 - (b) meningitis of the swineherds
- (2) secondary virus meningitis
 - (a) meningitis in connection with parotitis
 - (b) meningitis herpetica
 - (c) meningitis in connection with herpes zoster
- (3) meningitis allergica

Pette points out that the group of secondary virus meningitis includes also those forms of meningitis found in connection with poliomyelitis, epidemic cerebral inflammation, measles and chicken-pox, but gives to them no independent position owing to their isolated character. *Pette* regards the meningeal manifestations appearing in conjunction with virus diseases as forms of secondary virus meningitis, whereas those forms of meningitis are primary in which the symptoms caused by the virus in the organism remain more or less in the background in comparison with the meningeal symptom, or in which no such symptoms are present. In some cases it is extremely difficult to draw a boundary-line between these two groups, particularly with regard to the abortive forms of poliomyelitis in which the differential diagnosis towards idiopathic aseptic meningitis is sometimes based on more general epidemiological findings.

According to *Pette* the idiopathic aseptic meningitis is always a primary virus disease. As a rule it begins with a naso-pharyngeal infection and after a short period of latency the symptoms of an acute meningitis set in: rise of temperature, headache, nausea, vomitings, often stiffness of the neck. In case there are symptoms of an organic nerve lesion, e.g. paralysis of the optic muscle, changes in the optic nerve, etc. *Pette* regards these as symptoms of poliomyelitis or some disease of the encephalomyelitis group. As a rule there are great changes in the spinal fluid in the first stages of the disease: rise of pressure, increase of lymphocytic cells, decreasing, however, in about a fortnight to a normal state; simultaneously an increase of the protein content, which reaches its maximum later and is found for some time after the disappearance of the cells.

Pette was the first to use the diagnosis meningitis allergica. In his opinion there are some forms of meningitis in which the virus etiology is not quite applicable. Such cases are, e.g., those reported by *Bannwarth*. He refers at the same time to his observations regarding the etiology of the so-called Entmarkungsencephalomyelitis (EEM) and the etiology

of polyneuritis, in which allergic phenomena, as he thinks, are of decisive importance.

Bannwarth, the first to suggest the possibility of a rheumatic etiology in the pathology of meningitis, draws a number of rather daring conclusions. In his opinion the aseptic meningitis reported by *Wallgren* is the same as the rheumatic infection and thinks that the so-called *Guillain-Barré* symptom (increased protein content and simultaneously a normal or slightly increased number of lymphocytes in the spinal fluid = the G-B symptom) is the same as the serous inflammation reported by *Eppinger*. *Bannwarth* further suggests that the rheumatic inflammation spreads in the region of the meninges in the following manner: "Sitz des Rheumatismus war die Wirbelsäule mit ihren Bindegewebsapparate und Nerven-gestrüpp. Hier in Rückgratmesenchym wurden die Nerven nach ihrem Austritt aus dem Wirbelkanal von der rheumatischen Entzündung ergriffen und heftige Neuralgien waren die Folge. Im ersten zur Klinik-aufnahme führenden Schub hatte die rheumatische Entzündung eine besonders grosse Durchschlagskraft entwickelt, denn sie hatte nicht einmal vor der meningealen Barriere Halt gemacht, sondern sogar die Liquor-schranke durchbrochen und sich bis auf die weichen Häute des Rückenmarkkanals ausgebreitet."

The material at the disposal of *Bannwarth* includes 7 cases in which the patient had "rheumatic" or neuralgic pains and in which the liquor finding was surprisingly large and the recovery rather slow. As a rule there were rheumatic pains in the anamnesis and in some cases a focal infection was found. As a second group *Bannwarth* presents 6 cases of paralysis of the facial nerve in conjunction with benign aseptic meningitis. In these cases the pathological picture of the meningitis corresponds to the cases of the first group. *Bannwarth* regards these cases as essentially similar to the aseptic meningitis reported by *Wallgren* and in his opinion they are rheumatic in character.

In the second part of his investigations *Bannwarth* discusses the G-B symptoms in some forms of polyneuritis and polyradiculitis and concludes that this change of fluid is similar to the serous inflammation reported by *Eppinger*.

In a later work *Bannwarth* presents 3 additional groups of cases in which special attention has been paid to focal infections. In the first group there are mononeuritic conditions. The second group includes cases of multiple neuritis of the cerebral nerve, and one case a clear rheumatic anamnesis (polyarthrititis) and a remitting paresis. The third group includes radiculitis and chronic lymphocytic meningitis. On the basis of the cases reported by him, *Bannwarth* concludes that they are rheumatic and to support his view he points out that most of the patients were rheumatic, having suffered for many years from rheumatic pains. Further, focal

sepsis was present and the cases responded favourably to rheumotherapy.

It should be noted that *Bannicarth's* material includes chronic cases in which there is no clear evidence of the usual symptoms of acute meningitis and in which the duration of the disease is longer than that of benign aseptic meningitis.

It should further be noted, that most of these forms of meningitis are not isolated cases. *Bannicarth's* first heading to his comments runs as follows: "Über die chronische lymphocytäre Meningitis mit dem klinischen Syndrom der »Neuralgie« bzw. »Neuritis« und über ihre Beziehungen zum Rheumatismus." Later, he changed his attitude and used the heading: "Facialisneuritis mit dem Liquorsyndrom der lymphocytären Meningitis." He has thus left his original subject and is now dealing with a wider question, the relations between disorders in nervous tissue and rheumatic infection.

Schaltenbrand has some casual remarks on the matter. Some of his cases of polysclerosis in their initial stages show symptoms of benign-looking meningitis but later assume a definite character of polysclerosis. In his material we find 4 cases in which the above-mentioned development does not take place. In these cases the symptom of meningitis either disappears or remains as an isolated phenomenon.

These cases are:

No. 24, a male of 42 years. After a sudden onset with rheumatic symptoms a violent meningeal irritation rather surprisingly occurred two months later. The cell count rose to 5024/3. Roentgen-treatment produced good results in a couple of months.

No. 25, a female of 63 years. Aseptic meningitis with doubtful symptoms of polysclerosis. All the changes disappeared in a few months.

No. 26, a male of 22 years. Persistent aseptic meningitis, the cell count being for more than a year about 1000/3.

No. 27, a male of 31 years. In addition to polyneuritis the patient had intermittent pyramidal symptoms and increased content of cells and protein in the spinal fluid. The changes disappeared in a few months.

Schaltenbrand suggests that one heading is not enough to cover all forms of aseptic meningitis, some of the chronic cases showing a tendency towards polysclerosis and some towards polyneuritis. As to the etiology the author maintains the virus theory, but admits the possibility of a rheumatic etiology as well.

In their research on the various forms of polyneuritis *Schamburów* and *Lochowskaja* have come to the conclusion that the G-B symptom associated with them is due to the combination of a local venous stasis and a disturbance in the resorption of the liquor, and that the process concerned must be extradural and in the immediate neighbourhood of the subarachnoid. Further, that while the process is spreading in the sub-

arachnoid, there is evidence of pleocytosis and that the process in the extradural part of nerve roots and in the spinal ganglion may cause reflectory irritation in the meninges and result in a benign form of pleocytosis.

Sundelin has quite recently shown that in connection with polyarthritis pathological changes take place in the spinal fluid to the extent of 46.8 per cent. of the total number of cases.

Roeder and *Rehm* have found changes in spinal fluid similar to those occurring in benign aseptic meningitis, e.g., in essential hypertension, cerebral arteriosclerosis, encephalomalacia, nephritis and myxedema. Well-known are the symptoms of meningitis due to internal worms and also in connection with some poisonings, especially with lead-poisoning.

The classification meningitis serosa has recently been more or less abandoned. This symptom was reported by *Quinke* and its only really important feature was the increase in fluid pressure. This classification term has since then been used in various meanings and *Pette* suggests that the term be completely dropped, being, as it is, ambiguous and out-of-date. *Lange* uses the term side by side with arachnitis adhaesiva and regards this as a separate form of meningeal inflammation. As a rule this inflammation is chronic and appears in connection with cranial traumas and in infections causing a lesion of the local arachnoid and dura. The circulation of liquid is disturbed and there is evidence of cyst formations. According to *Weber* the etiology in these cases presents a wide variety. He divides the disease into two groups, the primary and the secondary. The disease has practical importance because of the tumour symptoms, caused by cysts. In these cases there is often evidence of a pathological spinal fluid.

Pachymeningitis hypertrophicans should also be mentioned here. According to *Bodechtel*, lues plays a part in its etiology, but the possibility of a rheumatic etiology must be considered as well.

The meningitis reported by *Curschmann* should be mentioned as a separate form of disease. It appears in connection with a neurotic edema and *Curschmann* regards it as identical with this edema. He reports a case having serous meningitis seven times within the course of a year, with simultaneous hemorrhage in the conjunctiva. Death occurred with meningeal symptoms.

The benign aseptic meningeal symptom has been discussed in the most diverse connections. The pathological picture is very complex and it is difficult to draw clear dividing lines. As mentioned above, the literature dealing with the acute forms of this disorder is abundant, whereas the chronic aspects have so far been discussed only in connection with other questions. This

fact seems to justify the presentation of a few cases of benign meningitis showing evidence of a chronic course and of reasonable independence. This will throw more light on the interesting question of the existence of a really independent chronic benign meningitis.

With this object in view I have read through the hospital reports of the Lapinlahti Hospital (= LH) starting from 1931, and I present here the cases of meningitis showing a benign character and a chronic course.

Case I. No. 643R/40. A stoker's wife, I.S. of 50 years. Heinola. Diagnosis: Meningitis chr.

For 20 years she had pains in the back. The pains were brought on when she pushed the boat afloat. The pains were worse in cold weather. Her teeth had always been bad and 15 years ago a tooth with pus in the root had been extracted. In autumn 1939 she had pains in the upper abdominal muscles. In March 1940 she travelled on the top of a timber-lorry and immediately afterwards she had severe pains in the chest and the back. In the following October she made a journey in a draughty train and the pains grew worse. She was admitted to the Surgical Hospital and kidney or biliary pains were suspected. Nothing, however, was found and the patient was transferred to LH. Here the temperature was normal, the left patellar reflex livelier than the right one, on the right side in the CIV-d III region reduced susceptibility to pain. Rate of sedimentation 10/24 mm. RR 120/90 mmHg. Wassermann —, Kahn —. The spinal fluid:

11.11.40	lumbar fluid:	Q—.	P+++ N+++,	cells 275 (big and small lymphocytes, a few leucocytes)
				WaR —.
26.11.40	"	"	P+++ N+++ Bact.—,	cells 142 (as before)
5.12.40	"	"	P+++ N+++	cells 47 (as before)
16.12.40	"	"	P+++ N+++	cells 75 (only lymphocytes)
27.12.40	"	"	P+++ N+	cells 29 ..
7. 1.41	"	"	P+++ N+	cells 31.5 ..
8. 1.41	"	"	P+++ N+	cells 27 ..
			(blood in the lumbar channel)	
15. 1.41	"	"	P+ N+	cells 42 (lymphocytes and old erythrocytes)

Discharged from the hospital 18.1.41.

Later examination 16.1.45. After leaving the hospital the patient had

for a few months a peculiar sensation in the right lower extremity. In both hands a sensation of cold and intermittent tenderness. In the right ear intermittent buzzing and sounds resembling the ticking of a clock. In the region of the liver and in the left shoulder rheumatic ache. She stands neither sunshine nor Finnish steam-bath, feels giddy, has headache and vomitings. Her hands are easily numbed. Two years ago during the whole summer, if she shut the left eye, she was unable to open it without the help of the hand. Blood pressure 155 mmHg. Blood picture normal. Physically fit. On neurological examination nothing positive was found except for a marked sensibility to touch in the right plexus brachialis, where she feels a radiating pain in the region of the liver. The pain is similar to that treated earlier in the hospital.

The spinal fluid in 17.1.45 in the lumbar fluid P+ N—, protein 19.6, cells 0.2. Wassermann —.

Discussion of the case:

1. Symptom of meningitis obviously benign. Duration exceeds that of the usual aseptic idiopathic meningitis, lasting for two months and showing evidence of a marked lymphocytosis. The onset of the disease, in spite of the acute symptoms, is not that of a typical meningitis. The symptoms are rather those of an acute radiculitis. At the time of the onset the patient had obviously no acute infection, on the basis of which it might be regarded as a primary or secondary virus meningitis. There is no rise of temperature and the rate of sedimentation is low.

2. There is no evidence of chronic disorders (hypertension, arteriosclerosis, diabetes, etc.) associated with changes of fluid of this kind. Therefore it cannot be regarded as a complication of them. There was no evidence of rheumatoid arthritis.

3. Neurological symptoms remain in the background except for the pains. The case does not belong to the EEM-group, at least not clearly, and its later development has not resulted in polysclerosis. Instead of that there is a paresis (of short duration) of the optic nerve, appearing 3 years after the discharge. This rather suggests polyn neuritis.

4. The pathological picture of the case is closely associated with the cases of neuralgia reported by *Bannwarth*. Long aching anamnesis, neuralgic pains and isolated paresis of the ocular muscle are characteristic features of it.

Case II. No. 79/35 and 632 R/37. Day-labourer V. B. of 42 years. Tikkurila. Diagnosis: Reactio psychogenea (hysteriformis)? Constitutio psychopatica (aggressive-querulous). Meningitis levis (serosa).

The patient's uncle died of diabetes. At the age of eight he had pneumonia, otherwise he has not been ill. He has never been to school, but can read and write. Married, three healthy children. His teeth have fallen out, one after another since 1932. In May 1934 his left arm was badly squeezed and got swollen up to the elbow. He was under polyclinical treatment in the Surgical Hospital. Diagnosis: Contusio antebrachi sin. Tenderness in the lower part of the left arm, the hand limp, fingers stiff and insensible (sensible only to heat). 18.8.1934 we find the following annotations at the polyclinic of LH: if the patient stretches out his hands, the left tends to drop; he can spread the fingers of the left hand only with difficulty. 7.11.1934 a circular boundary of sensibility is found round about the left elbow. Unable to spread the fingers of his left hand. He was admitted 15.1.1935 to the LH. The patient was found to be slenderly built, ill-looking, emaciated. Hb: 95 % Sahli. I: 0.95, E: 5.050 mil, L: 8060 (diff. nothing special). Urine: Alb —, Nyl +, Trommer + (on a later examination also the bloodsugar reactions were negative). Wassermann —, Kahn —. Neurologically: motor strength of the left wrist and the fingers lacking. Sensibility to pain, heat, and cold had disappeared from the left hand in a cuff-like manner, the boundary running about 3 inches distally from the elbow joint. Muscle reactions to faradic and galvanic current normal. The patient was discharged after examination. Later on, he has on several occasions undergone examination, both clinically and polyclinically. There have been slight variations in the boundary of sensibility in the left arm, and slight movements in the left hand fingers. No muscle atrophy. He complains of persistent headache, especially in bad weather. Other neurological findings negative. The spinal fluid:

4. 1.35 suboccipital		P++ N++Wbr++	cells 0.8
16. 1.35 lumbar	Q—	P+++N++Wbr+	.. 2.5
11. 4.35 „		P+++N++Wbr+	.. 4.0
30. 6.36 „		all changes as before	
3.10.37 suboccipital	Q—	P++++N+	.. 0.7
12.10.37 lumbar	Q—	P++++N++	.. 4.5
9. 5.40 suboccipital		P++ N+	.. 1.5
10. 4.42 „		P++++N++	.. 0.7
2. 1.45 „		P++++N++ prot. 130.0 mg%	cells 1.2

Wassermann always negative.

Discussion of the case:

1. Chronic nature of the symptom of meningitis is evident.

The time of onset is unknown, but the symptom has been followed for ten years and all examinations have revealed an obvious G-B-symptom.

2. The pathological picture in its development shows no associations with polyneuritis or EEM-process. Urine showed once a positive sugar-reaction and his uncle died of diabetes, but in all subsequent examinations there was no evidence of diabetes. The meningitis cannot be regarded as a complication of some chronic diseases, as there was no evidence of anything chronic.

3. The part played by trauma in the origin of the symptom of meningitis is questionable, particularly as there is no evidence of a more serious nervous lesion in the injured extremity. To what extent the psychic reactivity of the patient is referable to the symptom of meningitis is an open question. In his connection I refer to Case V.

4. Later research has explained the patient's persistent headache as being most probably of a neuralgic character. The case cannot be associated with any other previously known group of meningitis. The nearest possibility is to classify it as meningitis allergica.

Case III. No. 264 R/44. Master of Arts, a female of 34 years. Helsinki. Diagnosis: Meningitis aseptica.

She has from childhood been liable to get headaches, and to catch cold easily. Menstruations irregular and scarce. In 1939 she had exanthema in the face and in the back. It was cured with folliculin injections. Menstruations became more regular, too. 14.12.44 the headache, which kept recurring every now and then, got particularly violent, but stopped after 4 headache pills. 15.12.44 it was so violent that she had to cry for pain. No nausea. She was admitted 16.12.44 to L.H. At times she was subfebrile. No neurological symptoms. The rate of sedimentation 12/32 mm. Wassermann —, Kahn —. RR 120/85 mmHg. The spinal fluid:

18.12.44	lumbar	P++N—	prot. 105.0 mg%	cells 17.5 (lymphocytes)	Wassermann —
21.12.44	„	Q— P++N+		cells 62.5 (as before)	
28.12.44	„	P++N+		„ 40.5 „ „	
17. 2.45	„	P+ N—	prot. 39.5 mg%	cells 14.6 „ „	

The patient was discharged 30.12.44.

In subsequent examinations which were continued till autumn 1945 she had at times fits of headache and of fatigue. Plexus cervicales and nn. suboccipitales very sensible to touch. 10.3.46: continuous physiotherapy has been administered in the form of massage, sweating, and heat. No headache during treatment. Menstruations irregular, exanthema in the face and occasional fits of fatigue. Neurological findings negative.

Discussion of the case:

1. The symptom of meningitis is not quite compatible with idiopathic aseptic meningitis. The initial symptoms have a more neuralgic character and the patient has no other symptoms of acute meningitis except for the intense headache. Moreover, the fits of headache are liable to recur. The percentage of cells in the spinal fluid remains increased rather long, longer than that of protein. There is no evidence of infection in the initial stages of the disease. The highest temperature is 37.5 C., the rate of sedimentation low.

2. The disease in its development shows no associations with any of the chronic disorders of the central nervous system with which it might be supposed to be connected. The case has nothing to do with a neurotic edema.

3. The meningeal symptom can hardly be directly associated with the chronic exanthema appearing before and after the long period of headache. The headache is obviously of a neuralgic type and physiotherapy had probably a beneficiary effect on it. We have here obviously a type of constitution whose susceptibility to reaction is rather marked, and which presents an obvious disturbance in the hormonal equilibrium. We have good reasons to classify this case practically as a meningitis allergica.

Case IV. No. 170 R/45. A farmer's wife of 54 years. Porvoo. Diagnosis: Meningitis aseptica. Sclerosis disseminata inc.?

The patient has had 8 confinements, all the children are alive and in good health. No menstruations for two years. During a great many years headache and gastric pains. A year ago she had a gastric ulcer and was hospitalized for 7 weeks. In the summer 1944 she had a violent headache and ache in the neck. In autumn 1944 she had pains in both extremities. Gradually increasing ache in the back and the neck lately. Headache. Feels giddy, after Christmas she has seen things double. Of late, vomitings. She sleeps badly. She was under medical treatment in the

local hospital, the lumbar fluid: P+ N+ prot. 273 mg%. Wassermann —. She was admitted to L.H. 25.1.45, her general condition was good, RR 145/100 mmHg, rate of sedimentation 6/14 mm. Hb: 75/87 % Sahli, afebrile. Neurologically: her walking was unsteady, both legs gave way in running, Romberg, pressing force was weak in hands, knee- and Achilles-tendon reflexes lively. The eye specialist report 24.1.1945: double pictures due to disturbance in the cooperation of the accommodation-convergence activity. The spinal fluid:

30.1.45 lumbar	Q— P+++N++	cells 94.5	(lymphocytes and few polynucle.)
			Wassermann —
7.2.45 suboccipital	P+++N++	„ 83	(lymphoc.)
6.3.45 „	P+++N++	„ 148	„ prot. 214 mg%.

Discussion of the case:

1. The initial stages of the pathological picture indicate a markedly chronic course except for the vomitings, the etiology of which can be associated with gastric disturbances. Other features of the anamnesis speak in favour of a chronic course. The change in the spinal fluid obviously being chronic supports this view, the cell count keeping rather high for more than a month. The subsequent course of the case illustrates well its benign character.

2. The differential diagnosis as to EEM-process process extremely difficult. No proven neurological symptoms, either separately or taken together speak absolutely for it. On the contrary the long anamnesis of aches makes it improbable, although aches are encountered in a few EEM-cases. The fluid-finding gives more evidence for EEM than for idiopathic aseptic meningitis. The differentiation in respect to other groups of disease presents no major difficulties. The case is related to *Schaltenbrand's* case No. 25.

Case V. No. 707 R/42. Male gardener of 36 years. Myllykoski. Diagnosis: Reactio psychogenea hysteriformis. Meningoencephalomyelitis diss. chr.

The patient had the first attacks in 1939 when he was called up for military service. He was exempted and admitted to an insane asylum

for the time 21.11.-16.12.39. He was quite well ever since until the attacks recurred at Christmas 1941. He was admitted to LH 26.11.42. He was hysterical, and afraid of being called up again. The thyreoid gland was enlarged and slightly nodulous. The lymphatic glands enlarged. Rate of sedimentation 4/7 mm. On neurological examination nothing pathological was found, knee reflexes rather lively. He was discharged 19.12.42 in a better condition. The spinal fluid:

30.11.42 lumbar P++ N+ prot. 93.7 mg% cells 0.3 Wassermann —.

The patient was well and fit until his son was drowned while he was trying to rescue the child. This developed a psychogenic reaction and he was admitted to the hospital 28.11.44. Neurological findings: knee-reflexes extinct. He recovered rapidly and has been well ever since. On a later examination 2.2.45 the knee-reflexes were found to be still absent. The spinal fluid:

28.11.44 lumbar P++++N++ cells 8 (lymph.) Wassermann —
2. 2.45 suboccipital P— N— „ 1 prot. 20 mg%.

Discussion of the case:

1. The chronic nature of the meningeal symptoms is obvious. It is a typical G-B symptom. A benign case.

2. Connection with the simultaneous psychic disturbance is possible, we refer to Case 1 in which a strong psychic reactivity was found. An organic although insignificant change in the nervous tissue indicates an abortive form of EEM rather than anything else; or it is neuritic or possibly radicular.

Case VI. No. 707 R/36. A baker of 27 years. Kuopio. Diagnosis: Meningomyelitis chr.

The patient in 1931 had influenza and inflammation of the middle ear, which recurred in 1935. In September 1936 he had a rise of temperature, headache, vomitings, vertigo, stiffness of the neck and paralysis of the left facial nerve. He was admitted in the beginning of November to the local hospital. The spinal fluid: P+ N+ cells 766 and 13.11.36 P++ N+ cells 375 (lymphoc.) Wassermann —. He was admitted 13.11.36 to LH and in the accompanying letter we find the following annotations: T 36.8 Hb: 82 % Sahli. E: 4.28 milj. L: 6100. Wassermann —, Kahn —, rate of sedimentation 3/6 mm. In LH his general condition was good, neurologically and ophtalmologically nothing to report, rate of sedimentation 4/10 mm. Botriocephalus latus. The spinal fluid:

18.11.36 lumbar P+++ N++ cells 780 (lymphocytes)
2.12.36 „ P+++ N+ „ 599 „

22.12.36	„	P++++ N++	„	346	„
8. 1.37	„	P++++ N++	„	220	„
22. 1.37	„	P++++ N++	„	281	„
15. 2.37	„	P++++ N++	„	476	(out of which 89 % were small lymphocytes, 3 % monocytes, 6 % polynuclear, 2 % eosinophiles.)
16. 3.37	„	P+++ N+++	cells	212.5	(lymphocytes).

The patient underwent a malaria treatment and was discharged in a better condition. 12.1.45 the patient notified the hospital that he had resumed work in 1937 and felt quite well. In spring 1938 a headache set in. It was found to be due to inflamed maxillary sinus, and disappeared without special treatment. He was called up in spring 1943 and served at the front in spite of a rise in blood-pressure. In June 1944 he was taken ill with inflamed maxillary sinus and was operated on. He was demobilised 15.11.44 and felt well afterwards. 10.1.46 he reported a similar headache as in 1936 and stiffness of the neck. Nothing is known about his later life.

Discussion of the case:

1. In the initial stage the disease has the symptoms of an acute meningitis, the later stages showing a chronic course. A benign case. Ten years later there is a relapse.

2. The paralysis of the facial nerve, which was of a temporary nature, occasioned the hospital to classify this case in the EEM-group. The diagnosis should have been meningoradiculitis chr. There was nothing to suggest encephalitis or myelitis. Radicular mononeuritis is quite possible. The possibility of an otogenic complication is excluded by the low rate of sedimentation, the normal content of leucocytes, and the lack of neurological symptoms.

3. The case is closely associated with the cases of paralysis of the facial nerve reported by *Bannwarth*. Rheumatic pains, however, are lacking in the anamnesis, but there is an extremely great predisposition to otorhinogenic infections. This might support the assumption of the part of focal infection in the etiology of the disease.

Case VII. No. 707 R/38. A female worker of 23 years. Kurkijoki. Diagnosis: Meningoencephalitis disseminata.

The patient used to be quite well. Sight bad for ten years, cannot

read ordinary writing. The eye-clinic report: Atrophia n. optici. (campi reduced, pupils pale, Vod = 0, Vos = counts fingers 4 m.) She was admitted to the LH 30.11.38, the report running as follows: general condition good, rate of sedimentation 43/81 mm. Neurologically: the right hand movement in walking reduced; walking blindfolded deviations to the right. Slight jerks in left nostril. Vibration of tongue suggestive of atrophy. Pupils obviously deformed. In the extreme leftward gaze oscillating movement. Reflexes normal. Hb: 75 % Sahli. I: 0.87, L: 5200. The spinal fluid:

5.12.38 lumbar Q— P++ N++ cells 41.5 (Lymphocytes), Wassermann —.

After a complete overhaul of the teeth the rate of sedimentation rose, but was at the time of his discharge 27.1.39 32/84 mm.

9.9.40 the patient was re-examined. Her condition was unchanged.

Discussion of the case:

1. Obviously a case of chronic benign meningitis. The picture clearly differs from idiopathic aseptic meningitis.

2. The case has been classified as belonging to the EEM-group, mainly on the basis of the atrophy of the optic nerve. The vague nerve-symptoms enumerated in the hospital report, do not suffice to justify this view. *Mareschani* and *Klinke*, in their investigations of the inflammations of the optic nerve, have come to the conclusion that 50 per cent. of the isolated (non-luetic) inflammations of the optic nerve involve changes in the spinal fluid. In 50 per cent. of these cases, however, the change differs in quality from the changes in EEM. The two authors hold that these are not real EEM-cases and that, contrary to previous assumptions, all inflammations of the optic nerve have not the course of an EEM-disease. If the optic atrophy of the patient were a symptom of EEM, the disease would in all likelihood have caused other typical symptoms. The status, however, has been unchanged for 12 years. Seen against this background the case cannot be regarded as a typical case of EEM. We cannot assume, either, that the optic atrophy and the meningeal symptom at the given moment had more organic connection with each other, which, however, does not exclude the possibility that their etiology is the same. The meningeal symptom is to be regarded in this case as comparatively independent.

The case is a transitional form between chronic meningitis and EEM.

SUMMARY

Out of the above-mentioned seven cases four are males and three females, their ages varying from 23 to 54 years. The patients have been under observation for periods varying from 1 month to 10 years. In all the cases we find an obviously chronic meningeal symptom. In one case only the initial symptom was similar to acute meningitis. In this case there was evidence of all the clinical symptoms of acute meningitis, but the later course of the disease was obviously chronic (Case No. VI).

The cases represent rather isolated forms of meningitis. Definite organic lesions of the nervous tissue are found in Case IV in connection with a passing one-sided paralysis of the facial nerve; in Case VII, developing an optic atrophy ten years before the symptom of meningitis; further in Case V, in which the knee-reflexes were absent. Other nerve symptoms are: in four cases persistent headache of a neuralgic character (Cases I, II, III, IV). In two cases psychopathic constitution and reactivity were found.

In two cases there is a typical G-B symptom: Case II, in which the fluid was examined 9 times during ten years. The content of protein was very high, the cell count normal. In Case V, examined every two years, there was an increase in the protein content, the cell count being normal.

In the rest of the cases the meningitis is lymphocytic, the cell count varying as follows:

Case I	142-42
„ III	105-14,5
„ IV	94,5-148
„ V	780-212,5
„ VII	41,5

The diagnostics of these cases present considerable difficulties. As far as the meningeal symptoms are concerned the cases can be regarded as benign, but in spite of this they cannot without further consideration be included in idiopathic forms of meningitis, in the etiology of which infections and acute symptoms are preponderant. They cannot be included, either, in those forms of meningitis which according to *Roecker* and *Rehm* appear in connection with certain chronic diseases. On the basis of fluid findings alone they cannot be put into the same category as the fluid changes in polyarthritis. It is a matter of opinion, even in Case VII, whether the cases should be included in the EEM-group or be regarded as forms of polyn neuritis. It is hardly correct to regard these forms of meningitis as an etiologically separate group of meningitis.

We must have recourse to a group of symptoms called by *Pette* *meningitis allergica*. Among the cases of meningitis presented by him the most isolated are those having the greatest number of connections, viz. the neuralgic, the neuritic, and the radiculitic.

Despite the seeming isolation of the cases, the nerve tissue is involved to such an extent that it cannot be definitely settled by clinical investigations which of the localisations is primary. According to the principle of *Schambrow* and *Lochowskaja* the process caused by the meningeal symptom should be situated extradurally or subarachnoidally, or in the peripheral part of the nerve root or in the spinal ganglion. It is only natural that the picture of meningitis should be somewhat different in each case. On the other hand we know that the changes in the spinal fluid are due to changes of the capillary partitions in the region of the meninges (*Scheid*).

From this point of view it is natural that the same insult is capable of causing most various pathological pictures in the central nervous system. It is very likely that the pathological phenomena in the region of the central nervous system are few in number with regard to their quality.

It seems probable that, all things considered, the above-mentioned chronic-looking forms of meningitis, even if they seem

isolated, are only monosymptomatic cases associated with the central nervous system, abortive forms, in which the progress of the disease has been, as it were, cut off.

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ON THE TENSOR FASCIAE LATAE REFLEX

BY

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INTRODUCTION

By the tensor fasciae latae reflex (t.f.l.r.) is understood an involuntary contraction of the m. tensor fasciae latae (t.f.l.) in response to a cutaneous stimulus.

It should be noted that the definition given above only requires a muscular reaction to a cutaneous stimulus, so that it will also be justified to speak of the t.f.l.r. in the so-called spinal-automatic states.

In the present publication it will be shown that a reflex contraction of the t.f.l. can also, in a certain number of cases, be elicited by a tap on the "tendon" of the muscle (the tractus iliotibialis), or by a tap on the periosteum. As these reflexes are exactly like tendon and periosteum reflexes, it was not considered practical to extend the definition so much as to include them in the t.f.l.r. (If so, the definition would not have been in conformity with the one given by Brissaud).

It was first attempted by means of examinations of persons with unaffected nerves to determine the normal t.f.l.r. and its variations; possible changes of the reflex in patients with known disorders of the nerves were then examined, and it was thus attempted to find the nerve path of the reflex and to ascertain

The Aarhus University prize paper in neurology, 1946, with a few alterations. The work was done at the Neurological Department of the Municipal Hospital of Copenhagen (Chief: Senior Neurologist Knud H. Krabbe, M.D.). The patients with unaffected nerves were, however, examined at the Roskilde County and City Hospital. (Chief Physician: J. E. Holst, M.D.).

whether certain changes of the reflex were associated with definite disorders of the nervous system.

ANATOMICAL AND COMPARATIVE ANATOMICAL NOTES

Topographically, functionally, and with regard to innervation the musculus tensor fasciae latae belongs to the gluteal musculature. A few authors refer to it as the m. glutæus ant. (*Bardleben*).

According to *Gräfenberg*, the entire musculature of the hip is developed from a conical mass of tissue which in human embryos measuring 11 mm. is intimately connected; in embryos measuring 14 mm. the t.f.l. has become separated from the lateral border of the gluteal musculature.

The t.f.l. is primarily inserted on the primitive trochanter major; having been differentiated from the gluteal musculature, it is inserted into the tractus iliotibialis.

The t.f.l. is of highly varying size in different animals; it may thus be mentioned that in frogs it constitutes a very prominent and independent part of the huge triceps femoris. In rabbits, on the other hand, it is a small, subordinate muscle, which is lost posteriorly in the glutæus maximus, anteriorly in the rectus femoris.

As already mentioned, the t.f.l. is developed simultaneously with the gluteal musculature. The glutæus maximus is homologous to the deltoideus; the t.f.l. is homologous to a variant of the deltoideus (*Eisler*). The question whether these homologous muscles display "homologous" reflexes will be dealt with below.

In the adult human being the t.f.l. is a rather small flat muscle, which originates from the labium externus of the iliac crest close to the anterior superior iliac spine. It is placed superficially in its entire course down to the insertion into the fascia lata, which passes on into the tractus iliotibialis (*Maisiatti*), the strong, fibrous band which extends downward to the tibia, where it is inserted on the tuberculum Gerdy.

The glutæus maximus also takes part in the formation of the tractus iliotibialis.

The t.f.l. is innervated through the superior gluteal nerve, which belongs to the fourth and fifth lumbar segments.

The action of the t.f.l. is flexion and abduction of the femur. By its traction on the tractus iliotibialis it is of importance to the erect posture.

It may be mentioned that the other muscles referred to in the following (the quadriceps, the adductors, the sartorius, and the muscles of the lower leg) are innervated from the spinal segments L2 to S3.

The sensitive nerves from the skin of the sole of the foot pass primarily to the segments L5, S1 and S2.

BRIEF HISTORICAL SURVEY

Mention will only be made of the works that have been published especially on the t.f.l.r. (and the plantar reflex), but it may just be mentioned that it was in 1881 that *Wernicke* described the normal plantar reflex and that, in 1896, *Babinski* published his observations of the dorsal motion of the big toe in lesions of the pyramidal tract.

The t.f.l.r. was first described by *Brissaud* in 1895.

Brissaud became aware of the fact that, on irritation of the sole, a contraction of the t.f.l. occurred in addition to the movement of the toes. This reflex is termed *le reflex du fascia lata*. In many cases there is also a contraction of the adductors of the femur, and of the sartorius.

The anatomy of the muscle is referred to and it is mentioned that the spinal area of the reflex is the fourth and fifth lumbar segments.

In his thesis of 1901 *Harald Munch-Petersen* pointed out that the plantar reflex must be considered "a joint, reflex-released muscle action on the whole of the extremity, the intensity of which is increased with increasing excitation and which has occurred by the action of a single reflex centre, its purpose being

to remove the sole of the foot from the excitation by means of withdrawal."

The t.f.l.r. is included in this larger group of muscular contractions, and the contraction of this muscle is especially conspicuous because of its superficial localization.

Munch-Petersen refers the centres of the skin reflexes to the cerebral cortex in the vicinity of the fissure of Rolando. This is based on the interdependence between skin reflexes and sensibility, on the uniform picture of voluntary and reflex-released contraction of the lower extremity in case of plantar excitation, and on the conformity of the plantar reflex with the gait.

In a couple of publications of about 1902 *Crocq* dealt with the t.f.l.r. and its relation to the plantar reflex (i.e. the reflex-released plantar flexion of the toes).

His findings were as follows:—

- (1) Cases with lacking plantar reflex and retained t.f.l.r.: polyneuritis—no doubt the alcoholic form.
- (2) Cases with impaired plantar reflexes and increased t.f.l.r.: compression of the spinal cord in the lumbar region.
- (3) Lacking patellar reflexes, increased Achilles tendon reflexes, impaired plantar reflexes, but increased t.f.l.r. are found in "*traumatisme de la moelle lombaire suivi de polynévrite*".

Crocq repeatedly stressed that the primary reaction to plantar excitation is movement of the toes, followed by contraction of the t.f.l.r., the sartorius, the adductors, etc.; but the t.f.l.r. appears as the first response in spinal automatism.

On the basis of his own (and *Chadzinski's*) examinations *Crocq* believed that the centre of the t.f.l.r. was to be found in the medulla in contrast with the normal plantar reflex, which passes via the cerebrum. For a number of examinations had shown that the t.f.l.r. was present in complete, transverse lesions of the spinal cord with lacking tendon and skin reflexes; in hemiplegia there is also often an increased t.f.l.r. of the paretic side. The localization of the centre in the medulla is thus based on examinations of patients with lesions of the pyramidal tract.

Renault (1903) found that the t.f.l.r. is extremely variable in cases of organic hemiplegia, but that it was impossible to find out the rules of the variability. In case of compression of the medulla above the fourth lumbar segment the t.f.l.r. is retained or increased, in case of compression at a lower level the reflex is absent.

In cases of peripheral neuritis with lacking tendon and plantar reflexes the t.f.l.r. is found to be retained or increased.

In 1912 *Sabatini* examined 158 persons, including 40 healthy, with a view to the t.f.l.r. He found it to be highly varying, often accompanied by contraction of the adductors and the sartorius; in 52 per cent., however, an isolated contraction of the t.f.l. was found, next in frequency was the t.f.l.r. + movements of the toes.

In hemiplegia the t.f.l.r. was present in 60 per cent. of the cases, but it was weak. In complete, transverse lesion of the spinal cord it was absent, in partial lesion it was varying. The reflex was absent in tabes. In cases of neuritis it depends on the sensibility, being absent in anaesthesia but present in hyperaesthesia.

Sabatini believed that the clinical importance of the reflex was reduced by its variability; he believed that its centre is situated in the cortex, as it behaves like the other cutaneous reflexes.

In his *Sémiologie* of 1926 *Dejerine* wrote that the t.f.l.r. must be unchanged in case of a positive Babinski's sign.

As will be seen, the clinical observations and the conclusions of the various authors are quite varying. There is no agreement as to the localization of the reflex centre. Whilst the spinal centres of the tendon reflexes under cerebral influence are agreed upon, there is no agreement in modern neurological literature as to the cerebral centres of the skin reflexes, although most authors consider them to be cerebral reflexes. — (See *J. A. Bumke's* *Handbuch der Neurologie*; in this work the reflexes are, however, considered to be subcortical reflexes, as they may be retained in anaesthesia of the cortex cerebri).

Russell-Brain, on the other hand, writes on the plantar reflex: "It appears to be a spinal segmental reflex involving the

first sacral segment of the cord and akin to the abdominal reflex."

Monrad-Krohn believes that the normal plantar reflex perhaps has a cerebral reflex arc, the efferent part of which is the pyramidal tracts, its afferent part being unknown; it may be a double path, perhaps uncrossed centripetal fibres in the columna posterior.

The solution of this problem of localization is of considerable theoretical interest, and it is in particular with a view to this that the present work has been made.

EXAMINATIONS OF PERSONS WITH UNAFFECTED NERVOUS SYSTEM

These examinations were made on one hundred patients with unaffected nerves and at all ages—from new-born to 80-year-old patients.

The number is fairly evenly distributed in the different age-groups; 25 patients, however, are one, or less than one, year, as there are special problems to be considered in the first year of life.

Great importance was attached to having the said 100 patients thoroughly examined—most of them having been examined several times—instead of having a larger but less thoroughly examined material.

The subjects were chosen among patients who did not display any signs of disorders of nerves, joints or muscles; patients with a thick plantar skin, with oedemata, or with affections of the skin were also left out.

All the patients were examined in the recumbent posture; much importance was attached to making the patients relax completely; in many cases they had to keep their eyes closed to avoid interference of voluntary movements.

For the purpose of determining the most suitable stimulus, experiments were first made with a number of subjects.

Mechanical, thermic, and electrical stimuli were employed.

The mechanical stimuli (a prick or a stroke with a not too

pointed wooden stick) proved to be suitable; thermic stimuli (heat or cold of 60° C. and 0° C., respectively) are unable to elicit the t.f.l. reflex, whereas cold is rather a good stimulus to elicit the cremaster reflex. The electrical stimulus, too, is suitable, but some patients have a certain fear of the electrical stimulus (and apparatus), and the apparatus is somewhat cumbersome, too.

Therefore, it was decided to employ the mechanical stimuli; as a single stimulus, a prick on the sole of the foot, and for summation repeated pricking or stroking on the sole. In persons with unaffected nerves the t.f.l. reflex is elicited only by irritation of the sole of the foot, in some by a single stimulus, in many, however, only by summation of the stimuli.

In all the subjects a picture of the excitability of the sole of the foot was drawn up, the extent of the muscular contraction having been examined with a constant stimulus. In this examination the stimulation fatigue must be considered. In spite of gliding transitions there was, however, so decided a difference in the excitability that it was justified to draw up zones of greater or less excitability.

When these zones of excitability found in the 75 subjects past one year are transferred to one diagram, the following conditions are found:—



In most persons the excitability is greatest on the medial aspect; here the skin is, as a rule, thinnest. The thin skin can, however, hardly be the only explanation of the great excitability, as this is not in exact conformity with the degree of thickening of the epidermis (e.g. on the toes). In so great a number as 17 out of 75 cases the excitability was found to be absolutely great-

est on the anterior pad, although the epidermis was far more thickened there than in the medial area.

An adequate plantar irritation causes the t.f.l. to contract; the contraction manifests itself as a retraction of the seat of the muscle. When the reflex is more marked, the entire tractus iliotibialis becomes tense and retracted, often resulting in medial displacement of the quadriceps; this displacement can, however, be easily distinguished from the contraction of the quadriceps, which may also occur in a number of cases.

A single stimulus applied to the sole of the foot causes a rather quick contraction of the t.f.l. (single contraction?); stroking of the sole first produces a contraction of the t.f.l., which then remains in a state of tonic contraction for some time, and, lastly, follows the phase of relaxation which is most often the most protracted.

With regard to the dependence of the contraction on the intensity of the stimulus, conditions are somewhat varying. A certain degree of stimulus is necessary to elicit the reflex; when the stimulus is increased beyond the threshold, the contraction will increase in a fairly direct ratio to the increase of the intensity of the stimulus, up to a certain upper limit in most individuals.

In most cases an increase of the stimulus will first and foremost cause the contraction to be prolonged; in particular the phase of relaxation seems to be prolonged with increasing stimuli.

In a number of cases the reaction is fairly independent on the intensity of the stimulus; in a few cases there is an optimum stimulus, so that both weaker and stronger stimuli give a weaker contraction.

The excitability varies somewhat in the same person under different conditions (time, fatigue, etc.), but still it is always of the same magnitude.

With very powerful stimuli the reflex becomes more complicated and the voluntary element becomes more difficult to exclude; the isolated reflex is most finely produced by moderate stimuli.

In all cases a fairly good conformity was found between the patient's sensation of ticklishness and the degree of excitability. However, the writer dare not establish any causal relationship between these two things on this basis.

In subjects past one year the t.f.l. reflex was found to be present in 73 out of the 75 cases. The two cases in which it was absent were that of a 17-year-old boy who could not be made to relax his tractus iliotibialis, and that of a subject, aged 24 years, who was not ticklish at all. In both of these cases there appeared a plantar flexion of the toes in response to the plantar stimulus.

In one of the 73 cases the reflex could not be observed, but on palpation of the muscle a reflex contraction could be distinctly felt.

The intensity of the contraction is independent of sex and age. The material has been divided into 3 groups; one with medium brisk reflexes, one with fainter, and one with stronger reflexes. The average age is the same in all the 3 groups.

Irritation of the plantar skin is capable of producing the following reactions:—

- | | |
|--|--------------------|
| (1) Contraction of the tensor fasciae latae: | 73 out of 75 cases |
| (2) plantar movement of the toes: | 73 " " 75 " |
| (3) contraction of adductors of the femur: | 35 " " 75 " |
| (4) " " the quadriceps femoris: | 10 " " 75 " |
| (5) " " the sartorius: | 9 " " 75 " |
| (6) " " the cremaster: | 3 " " 75 " |

Powerful stimuli cause dorsal flexion of the knee and the hip in a great number of cases.

On comparison between the t.f.l. reflex and the plantar reflex (meaning in the following the plantar movement of the toes after irritation of the sole of the foot), the results were as follows:—

In 10 cases the t.f.l.r. was > the plantar reflex
 .. 7 " " t.f.l.r. " > " " "

In 7 cases the plantar reflex was $>$ the t.f.l.r.
 „ 2 „ „ „ „ „ $>$ „ t.f.l.r.

In the remaining number of cases the t.f.l.r. was $=$ the plantar reflex.

The comparison was made by examining which of the reflexes had the lowest threshold stimulus, as it was considered that no direct comparison could be made between the contraction of a muscle and the movement of a toe.

The stimulation fatigue of the t.f.l. reflex was examined by determining how many times the reflex could be elicited by strokings in rapid succession on the sole of the foot.

In more than half the number of cases the stimulation fatigue was slight, as the reflex could be elicited fifty times or more in succession. In about 30 per cent. of the cases the t.f.l. reflex faded away before it had been elicited ten times.

A rapid stimulation fatigue has previously been pointed out as being characteristic of skin reflexes in contrast with tendon reflexes. The stimulation fatigue of the t.f.l. reflex does not seem to be more marked than that of the patellar reflex. The abdominal reflex, on the other hand, is fairly soon fatigued.

In 2 out of 75 cases a tap on the distal part of the tractus iliotibialis produced a distinct reflex contraction of the t.f.l. reflex; in 3 of the cases a tap on the lateral femoral condyle elicited a reflex contraction of the t.f.l.

For purposes of comparison the following reflexes were examined in all the patients:—The abdominal reflexes (the ordinary 3 on either side), the cremaster reflex in males, the patellar reflexes, the Achilles tendon and the palmar reflexes. The so-called cremaster reflex in females seems to me to be too inconstant to be of any interest.

The abdominal reflexes were present in 70 out of 75 cases (the remaining 5 patients had large and flaccid abdominal walls).

The cremaster reflex was present in 56 out of 58 cases; it was elicited from the sole of the foot in 3 cases (all the 3 under 30 years of age).

The patellar reflex was lacking in one out of 75 cases.

The Achilles tendon reflex was lacking in one out of 75 cases and was doubtful in one case.

On irritation of the skin in the palm of the hand no reflex of constant occurrence was found; in particular no reflex-released contractions were observed in muscles of the shoulder region, which, as is known, are homologous to the t.f.l.

No direct connection has been demonstrated between the presence and intensity of the various reflexes.

The t.f.l. reflex and the plantar reflex are roughly present at the same time; as already mentioned, one may be absent when the other is present, and their intensity may vary independently.

No connection has been demonstrated either between the tendon reflexes and the t.f.l. reflex; in the cases where the t.f.l. reflex is lacking, the tendon reflexes are present and *vice versa*; any unquestionable connection between the intensity of the two groups of reflexes has not been demonstrated either.

EXAMINATIONS OF CHILDREN FROM 0 TO 1 YEAR OF AGE

This group comprises 25 children.

The youngest in this group (about the first 6 months) show rather uniform conditions, as plantar irritation produces flexion of knee and hip, and Babinski's sign. The t.f.l. occupies a very conspicuous position in the reflex-released muscular contraction, but almost all the subjects also display contraction of adductors and flexors of the femur.

The reaction was released by very weak stimuli, and one or more almost always gave rise to crying and to warding-off movements.

It was very difficult to examine the stimulation fatigue, and examinations of plantar zones of varying excitability had to be made in oft-repeated excitation experiments.

The excitability for the t.f.l. reflex seems to be rather uniform all over the sole of the foot; it was not possible at any rate to demonstrate the difference of excitability ascertained in adult patients. As already mentioned, examinations of excitability in these small children are beset with great difficulties, so that safe conclusions cannot be drawn from the differences demonstrated between infants and adults; of course it suggests itself to connect the differences with the gait.

In the group of children the abdominal reflexes were only present in one case; the cremaster reflex was almost always present. It should be borne in mind that the abdomen of children who are a few months old is often large and somewhat distended.

The patellar reflex could be elicited in all cases; there were no extended reflexogenic zones or patellar clonus.

It may be mentioned as a matter of curiosity that a reflex examination was made in a child about 5 minutes before delivery, as there was prolapse of one of the legs. The reaction to the plantar stimulus was exactly like that seen in infants.

The second half of the first year of life appears as a transition from the above-mentioned picture in children under 6 months to the one demonstrated in adult patients.

The t.f.l. reflex becomes more conspicuous and isolated; the warding-off movements become less marked, the abdominal reflexes increase in frequency and the excitability of the sole of the foot approaches that of adults. Babinski's sign is still present.

EXAMINATIONS OF PATIENTS WITH ORGANIC NERVOUS DISORDERS

This group comprises 85 patients examined, including
a few children.

(1) *Disorders of peripheral nerves and of the muscular system.*

In cases with anaesthesia of the reflexogenic zone the t.f.l.r. was found to be suspended. As an example mention may be made of a patient, aged 76 years (diagnosis: Neuritis n. tibialis dxt.

e varicibus et ex injectione in varic.), with anaesthesia and analgesia of the sole of the right foot, paresis of the plantar flexion of the right foot and toes, but no paresis of the femoral muscles.

In this case there was no t.f.l.r. on the right side, whilst it was present on the left side.

Similarly it has appeared that in patients with local anaesthesia of parts of the sole or of toes, the t.f.l.r. could not be elicited from the anaesthetic zone, even if it could be before the anaesthesia was produced.

Two cases of polyradiculitis (Guillain-Barré) may be mentioned as examples of disorder of the motor neuron. In these cases there was paresis of the lower extremities with suspended tendon reflexes, but retained sensibility to touch and pain. Plantar irritation produced no reaction.

A combination of disorders of sensitive and motor radices was found in efficacious spinal anaesthesia. In these cases the t.f.l.r. was found to be suspended.

Conformity was ascertained between sensibility and the t.f.l.r. in all cases but one, which will be briefly reported:—

It was the case of a man, aged 70 years, who had an atypical polyneuritis manifesting itself as hypaesthesia and hypalgesia in part of the left lower extremity, including the sole of the foot; in spite hereof the t.f.l.r. was found repeatedly to be far more pronounced on the left than on the right side. (Thus there is no absolute conjunction between sensibility and the t.f.l.r., cf. Munch-Petersen's thesis).

Conclusion: In disorders of the sensitive or the motor neuron of the reflex arc causing the nerve conduction to be discontinued, the t.f.l.r. is found to be suspended.

In cases of affection of the musculature with normal sensibility, the intensity of the reflex is found to be reduced in accordance with the impairment of the musculature. In this group a number of patients with progressive muscular dystrophy and inactivity atrophies were examined (the latter being due to unilateral protracted immobilization, e.g. after fracture).

(2) *Affections of the spinal cord.*

These include compressions of the cord (traumatic, tuberculous spondylitis), tumours of the cord and transverse myelitis, a total of 10 cases. It was attempted in particular to have patients examined in whom the nature and degree of the lesion had been inspected at operation; some cases, however, have been included in which no such direct observation was possible. The material does not include any quite unquestionable case with lesion of the area from which the t.f.l. is innervated.

There are 3 cases of traumatic compression of the cord above the lumbar region, presumably with complete disconnection, all of them having been observed as long as possible. The cases are rather uniform, but with a certain difference as to time.

Example: A man, aged 26 years, had his tenth thoracic vertebra broken in a fall with a motorcycle; soon after admission to hospital, flaccid paresis of the lower extremities and suspended skin reflexes were ascertained. At operation the tenth thoracic vertebra was found to have been broken, and very considerable contusion of the cord was ascertained. Redressment and decompression were performed. On examination of the patient a fortnight later the condition was as follows: Plantar irritation produced slight contraction of the t.f.l. and of the flexors on the femur, but no movement whatever of the toes. The patellar and Achilles tendon reflexes could not be elicited; the upper abdominal reflex was faintly present, the sensibility suspended as far as to a few cm. below the transverse umbilical line. Subsequent examinations (throughout two months) showed fairly unchanged conditions, apart from dorsal movement of the big toes.

The two other patients also had traumatic lesions of the cord, one at the level of the sixth, the other at the level of the eleventh thoracic vertebra. The lesions of the cord were very deep, with yellowish disintegration to an extent of several centimetres. With regard to reflexes, conditions were as in the case described above. Plantar irritation produced contraction of the t.f.l. and of the flexors, later Babinski duplex. Tendon reflexes

could not be elicited. The cases were examined up to 3 and 4 months, respectively, after the trauma.

As examples of partial lesions of the cord there are two cases with extirpated neurinomata in the cervical region and two cases of tuberculous spondylitis in the same region. In these cases there were marked t.f.l. reflexes which, besides from the sole of the foot, were elicited from large parts of the lower extremities; plantar irritation also produced Babinski's sign. There was some tendency to flexion of the knee. Also, spasticity of the lower extremities.

Transverse myelitis: Lastly, mention may be made of the case of a man, aged 51 years, who suddenly had intense pain round the umbilicus four days before admission, a few hours later flaccidity of the legs and retention of the urine.

On admission there was completely flaccid paresis of the lower extremities without any response to plantar irritation; 15 days after the onset of the disease there was isolated and distinct t.f.l.r. on plantar irritation, but no movement of the toes; tendon reflexes could not be elicited either.

Some weeks later, plantar irritation also elicited movement of the toes (brisk warding-off, but no doubt Babinski duplex). Gradually the power of the legs became fairly good.

Patients with disseminated sclerosis are mentioned in a separate group.

Conclusion: It was not possible during the limited time at disposal for the examinations to follow the patients for so long a time as might have been desired. In return the material comprises patients with identical disorders in which, however, the time of onset before examination differs, so that the patients considered as a whole afford a picture of how conditions must be supposed to be when one patient is followed for a prolonged period.

After a—presumably complete—lesion of the cord above the lumbar region there is flaccid paresis of the lower extremities, without any response to plantar irritation, after some time the t.f.l.r. can be elicited, isolated or with simultaneous contraction of flexors; Babinski's sign does not appear until later.

In partial lesions of the cord above the lumbar region the lower extremities are found to be spastic, with marked t.f.l.r. In addition to contraction of the t.f.l. there is positive Babinski's sign and other spinal automatic reflexes.

(3) *Cerebral disorders.*

The examination of 18 patients with hemiplegia following apoplectic fits will be mentioned first. The cases are stated in the following table. One patient is one day old, one is 3 weeks old, all the others are older patients.

One patient, not included in the table, was examined in the comatose stage of a cerebral hemorrhage; about half an hour after the onset spontaneous jerking of the lower extremity was observed, ceasing when the etherdown was removed. Irritation of the lower extremity produced Babinski's sign and contraction of the t.f.l. simultaneously with flexion of the knee. Abdominal and cremaster reflexes were not present.

The patient was repeatedly examined, the coma deepened and ended fatally in the course of twenty-four hours; simultaneous gradual decrease of the reflex activity.

Groups I and II: see following tables.

Group III:

This group comprises 3 patients whose condition changed much in the course of examination, so that the reflexes varied much in the different examinations.

Conclusion: The findings on the spastic side in hemiplegias were as follows: In 12 cases increased t.f.l.r., in 3 cases decreased; the abdominal reflexes suspended or impaired in 14 cases; the sensibility decreased in all cases.

(4) *Disseminated sclerosis.*

The results of examinations of 12 patients with disseminated sclerosis are stated in the table below.

Hemiplegias Group I.

Ages	T.f.l.r.	Plantar.	Abd.	Crem.	Patel.	Achil.	Hemiplegia
70	r.: ++ l.: ++	B. dxt.	0 ++	0 ++	++ ++	? ?	dxt.
72	r.: ++ l.: ++	B. sin.	0 0	0 0	++ ++	+ ++ + Clonus	sin.
69	r.: ++ l.: ++	B. sin.	++ ++	++ ++	++ ++	++ ++	sin.
60	r.: ++ l.: ++	B. dxt.	0 0	0 0	++ ++	++ ++	dxt.
68	r.: ++ l.: ++	B. sin.	++ ++	++ ++	++ ++	++ ++	sin.
81	r.: + l.: ++	B. sin.	(+) 0	(+) 0	++ ++	? ?	sin.
69	r.: ++ l.: ++	B. dupl.	0 +	0 +	++ ++	++ ++ + Clonus of both	dupl.
82	r.: ++ l.: ++	B. dupl.	++ ++	++ ++	++ ++	(+) (+)	dupl.
64	r.: ++ l.: ++	B. dxt. (B. sin.?)	0 0	0* 0	++ ++	++ ++	dxt.
65	r.: ++ l.: ++	B. dxt.	0 0	0* 0	++ ++	++ ++	dxt.
65	r.: ++ l.: ++	B. sin.	0 0	0* 0	++ ++	++ ++ + Clonus	sin.
69	r.: ++ l.: ++	B. dxt.	0 +	0 +	++ ++	++ ++	dxt.

Hemiplegias Group II

Ages	T.flr.	Plantar.	Abd.	Crem.	Patel.	Achil.	Hemiplegia
83	r.: + l.: +++	B. dxt.	0 +	0 +	? ?	+++ ++	+++ dxt.
73	r.: ++ l.: +	B. sin.	+	+	+	+++ (+)	sin.
67	r.: ++ l.: ++	B. sin.	0 0	0* 0	♀ +	++ ++	++ sin.

* Abdomen fat. R. = Babinski.

Disseminated sclerosis.

Ages	T.f.l.r.	Plantar.	Abd.	Crem.	Patel.	Achill.
27	r.: + + + + + l.: + + + + +	B. dupl.	(+) (+)	0 0	+ + + + + +	+ + + + + +
16	r.: + + l.: + +	B. dupl.	+ + + + + + + + + +	+ + + +	+ + + +	+ + + +
39	r.: + + + + + l.: + + + + +	B. dupl.	+ + + + + + + + + +	+ + + +	+ + + + + + + + + +	+ + + + + + + + + +
41	r.: + + + + + l.: + + + + +	B. dupl.	0 0	0 0	+ + + + + +	+ + + + + +
53	r.: + + + + + l.: + + + + +	B. dupl.	0 0	0 0	+ + + + + + + + + +	+ + + + + + + + + +
31	r.: + + + + + l.: + + + + +	B. dupl.	+ + + + + + + + + +	+ + + +	+ + + + + + + + + +	+ + + + + + + + + +
35	r.: + + + + + l.: + + + + +	B. dupl.	0 0	0 0	+ + + + + + + + + +	+ + + + + + + + + +
33	r.: + + + + + l.: + + + + +	B. dupl.	+ + + + + + + + + +	0 0	+ + + + + + + + + +	+ + + + + + + + + +
46	r.: + + + + + l.: + + + + +	B. dupl.	0 0	0 0	+ + + + + + + + + +	+ + + + + + + + + +
62	r.: + + + + + l.: + + + + +	B. dupl.	0 +	0 +	+ + + + + + + + + +	+ + + + + + + + + +
29	r.: + + + + + l.: + + + + +	B. dupl.	0 0	0* 0	+ + + + + + + + + +	+ + + + + + + + + +
63	r.: + + + + + l.: + + + + +	B. dupl.	0 0	0 0	+ + + + + + + + + +	+ + + + + + + + + +

* Abdomen fat.

Paralysis agitata.

Ages	T. ltr.	Plantar.	Abd.	Crem	Paral	
76	r.: ++ l.: ++	+	++ ++	++ ++	0 → ++ 0 → ++	tonus increased alike on both sides
67	r.: ++ l.: ++	?	++ ++	++ ++	++ ++	tonus increased alike on both sides
65	r.: ++ l.: ++	(++) (++)	0 0	0 0	++ ++	tonus most increased on r. side
65	r.: ++ l.: ++ → (++++)	+	0 0	0 0	++ (++)	tonus most increased on l. side

Encephalitis epidemica chronica (Parkinson).

70	r.: +++ l.: +++	++ ++	+++ +++	+++ +++	+++ +++	++ ++	rigidity alike on both sides,
44	r.: ++ l.: ++	++ ++	++ ++	++ ++	++ ++	+++ +++	tonus nat.
52	r.: +++ l.: +++	+++ +++	(++) (++)	(++) (++)	0 0	+++ +++	tonus most marked on r. side.

It will be seen that there is a marked connection between the t.f.l.r. and spasticity, the reflex being strongest when the spasticity is most pronounced. The t.f.l. reflexes are increased in 8 out of 12 cases, 10 of which display spasticity of the lower extremities, (the t.f.l. reflexes are more marked than in the normal material), in 2 cases with different spasticity of the two legs the t.f.l.r. is found to be most marked on the spastic side.

The abdominal reflex is lacking in 6 out of the 12 cases, uncertain in 3 and normal in 3 cases. The cremaster reflex is lacking in 6 cases and normal in 6.

In all the patients in whom the t.f.l.r. is elicited outside the sole of the foot the zone is the same as produces Babinski's sign.

(5) *Patients with rigidity.*

In all the 7 patients with rigidity the t.f.l.r. is well marked; in 2 of the cases the rigidity of the legs differs, the t.f.l.r. being most marked on the most rigid extremity. (*Monrad-Krohn* demonstrated the highest increase of abdominal reflexes on the most rigid side in paralysis agitans).

(6) *Various disorders.*

In patients suffering from cryptogenic epilepsy no changes of the t.f.l.r. have been demonstrated, but I have had no opportunity of examining a patient in direct connection with a seizure.

In a group of patients with cerebral disorders other than those already mentioned (tumours, traumatic lesions, etc.) signs of changes of the t.f.l.r. were only found when symptoms of lesion of the pyramidal tracts could be demonstrated.

In two cases of gunshot lesions of the brain these have given rise to spastic hemiplegia, which behaved exactly like the apoplectic hemiplegias with increased t.f.l.r.

A patient with Jacksonian fits in the right lower extremity (diagnosis: *Aneurysma hemisphæri sin.*) responded to plantar irritation with isolated contraction of the t.f.l. of both legs. Such a reaction was not observed in any other case.

In 3 mild cases of locomotor ataxia normal t.f.l.r. and plantar reflexes were found.

A number of patients with poisoning due to abuse of hypnotics (5) and anaesthetized patients have been examined, having been followed from hour to hour. The t.f.l.r. is suspended rather late, later than the plantar reflex, but at much about the same time as the patellar reflex.

CONCLUSION AND DISCUSSION

It has been shown by repeated examinations that the t.f.l.r. is a reflex of fairly constant occurrence in adults (lacking in barely 3 per cent. of the cases). It varies somewhat in different individuals; it is always unchanging in the same individual.

In persons with unaffected nerves the reflex can be elicited only from the sole of the foot; when elicited from zones outside the sole, it is suggestive of a lesion of the pyramidal tracts. In such cases the t.f.l.r. could always be elicited from the same zone as Babinski's sign.

The t.f.l.r. and the plantar reflex occur with much the same frequency in the patients examined, which is at variance with what has been stressed by previous authors, that the plantar reflex is of primary occurrence.

The stimulation fatigue of the t.f.l.r. is not particularly great, not greater than in the case of the patellar reflex; however, I do not venture to ascribe any great importance to this fact.

Lastly, it has been shown that in a small number of cases the t.f.l.r. can be made to join in a tendon or periosteal reflex; the same applies to the adductors of the femur (quite frequently) and to the quadriceps femoris.

In most cases with spasticity the t.f.l.r. is found to be increased, mostly so in cases with the greatest spasticity. In these patients there is a marked difference between the t.f.l.r. and the abdominal-cremaster reflexes.

In complete transverse lesion of the cord all reflexes have

been suspended; when they recur, the t.f.l.r. is the first to appear. No cases with retained tendon reflexes and suspension of the t.f.l.r. have been ascertained.

These findings show that the t.f.l.r. can be elicited via a centre of the spinal cord in case of lesions above the lumbar region.

Whether the reflex has a cortical centre in addition to this medullary centre (like the abdominal reflex), cannot be decided with certainty; for there is a certain difference in relation to the abdominal reflex (still, spinal-automatic reflexes have also been described in the case of the abdominal reflex (*Dejerine, Monrad-Krohn*)). A number of facts speak in favour of the presence of a cortical centre under normal conditions, *inter alia* the connection between sensation and reflex (however, there need not be any causal connection). It is worth noticing that in lesions of the cord above the lumbar region, or of the brain, no cases have been demonstrated in which the tendon reflexes (supposed to have their centre in the cord) were retained and the t.f.l. reflexes suspended. If there are two centres (a medullary and a cortical one), the reflex elicited by either of these routes is much the same, but in case of lesions of the pyramidal tracts the t.f.l.r. can be said to join in reflexes of the ordinary spinal-automatic type. It cannot be said whether any change of the contraction of the muscle would be possible at all in either of these cases.

Besides in spasticity an increased t.f.l.r. is also found in case of rigidity; according to the current view, the modes of occurrence of spasticity and rigidity are quite different, but perhaps it is just so that the muscle with changed tonicity (the spastic as well as the rigid muscle) gives a stronger response to a given stimulus, the reflex gives a greater deflexion; that this changed form of tonus is of cerebral determination, is another aspect of the same matter.

Clinical importance: A certain level-diagnostic importance is associated with suspension of the reflex; when elicited outside the sole of the foot, it is pathological (lesion of the pyramidal tracts). In transverse lesion of the cord the t.f.l.r. is the first

to recur, this seems to be so also in case of poisoning with hypnotics.

It is an advantage that the t.f.l.r. can be very easily observed.

It was hoped that it would be possible in the present work to carry out a number of electrical examinations.

An electromyographical examination of the reflex would have been of interest, since it would then be possible to see whether it is the same motor units that function when the muscle is acting as a cutaneous reflex and as a tendon reflex.

With regard to the localization of the reflex centre, it would be of interest to be able to measure the latent period of the reflex contraction of the t.f.l. in response to a cutaneous stimulus and to a tap on the tendon, as it must be taken for granted that the centre of the tendon reflex is to be found in the cord. In an examination of this nature it would, of course, be a necessary condition that we could acquire a knowledge of the rate of conduction of the nerves involved and the latent period of the sensitive end-organs. It would perhaps be better to try to find whether the latent period of the t.f.l.r. differs in lesions of the pyramidal tracts and in persons with unaffected nerves; by means of such an examination it would undoubtedly also be possible to illustrate the problem of the localization of the centre.

I hope I shall be able to publish such examinations in a subsequent work.

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THE CEPHALIN-CHOLESTEROL FLOCCULATION TEST (OF HANGER) IN PSYCHIATRY

BY

N. SPEIJER

In 1938 *P. M. Hanger* (1) introduced the cephalin-cholesterol flocculation test as a means of detection of hepatogenous damage. Cholesterol with cephalin from sheep brains is mixed in an emulsion with 0.2 cc serum and after 48 hours gives a flocculation varying from 0 to + 4. The working or mechanism of the reaction is unknown, but should be connected with certain globulin fractions in the serum. *H. de Jong*, who has already worked several years in the field of experimental catatonia and who considered these a general reaction form of the central nervous system, also, after experimental influencing of the functioning of the liver in animals, saw catatonia assert itself. He and *J. Harold St. John* (2) investigated the effect of the cephalin cholesterol flocculation test with catatonia, with other forms of schizophrenia, and with other psychoses.

The technique is fairly simple. The cephalin-cholesterol antigen (Difco Laboratory Inc., Detroit, Michigan) is supplied as dry stuff in small bottles. 5 cc. ether per bottle is added. 1 cc. of this solution is mixed with 35 cc. aqua dest. from 65-70° C. Then it is reduced by heating to 30 cc. Cooled to room temperature 1 cc. is added to 0.2 cc. serum, diluted with 4 cc. salt solution. No reaction and a flocculation of + 1 and + 2 is considered as not abnormal. Reactions of + 3 and + 4 count as positive.

De Jong and *St. John* examined 147 schizophrenics and 116 control cases (other psychoses and normal individuals). Their results, as far as they have informed us, have been combined in Table 1.

TABLE I
(according to *de Jong* and *St. John*).

Diagnosis	Numbers of cases			Pos. reactions			Pos. react. in %		
	m	w	T	m	w	T	m	w	T
<i>Schizophrenia</i>									
Catatonic			32			15			46,8
non-catatonic	56	59	115	9	25	34	15,2	44,6	29,5
			147			19			33,3
<i>Control group.</i>	m	w	T	m	w	T	m	w	T
epilepsia		26	26		0				
manic-depr. group			23			1			
other psychoses			15			1			
norm. individuals.			52			4			
			116			6			5,2

It appears from this

- (1) that schizophrenics give more positive reactions than the control cases (33.3 % : 5.2 %)
- (2) that catatonics give more positive reactions than the other forms of schizophrenia (46.8 % : 29.5 %)
- (3) that women schizophrenics give more positive results than men schizophrenics (44.6 % : 15.2 %).

Even when one realises that schizophrenia is a general name for the most heterogenous diseases, and that "catatonic form" is not always so easily distinguishable from other "forms", as is often the case (*de Jong* and *St. John* do not go into this matter, and their number of catatonics is rather small for determining differences), still this research could lead to important conclu-

sions, should their result be corroborated. According to them, as a result of their research, liver damage, i.e. changing of the liver functions, might possibly be a primary cause for the appearance of catatonic symptoms and at the same time might influence the appearance of other symptoms of schizophrenia. A continued study of this positive result of the reaction would then be indicated.

Hence, it seemed to me necessary to repeat their examination. My results are stated in Table 2:

TABLE II
(The writer's research).

Diagnosis	Number of Cases			Pos. reactions			Pos. react. in %		
	m	w	T	m	w	T	m	w	T
<i>Schizophrenia</i>									
Catatonic	32	16	48	7	3	10	21,9	18,8	20,9
non-catatonic	89	124	213	27	47	74	30,3	37,6	34,7
	121	140	261	34	50	84	28,1	35,7	32,2
<i>Control-group</i>	m	w	T	m	w	T	m	w	T
epilepsia	7	6	13	1	1	2			
manic-depr. group	17	30	47	5	7	12			
dem. art. et sen.	21	14	35	4	6	10			
oligophrenia	30	43	73	9	19	28			
other psychoses	19	20	79	7	4	11			
	94	113	207	26	37	63	27,7	32,8	30,5
norm. individuals	29	29	58	10	15	25			
	123	142	265	36	52	88	29,3	36,6	33,2

I examined 261 schizophrenics and 265 control cases (other psychoses and normal individuals). From Table 2 it appears that

- (1) in contrast to the *de Jong* and *St. John*, schizophrenics show nearly the same positive reactions as the control cases (32.2 %:30.5 %), including the normals 32.3 %:33.2 %).

This contrast results from the fact that the control group in my investigations gives more positive reactions than in those of *de Jong* and *St. John*.

- (2) in contrast to *de Jong* and *St. John* catatonics show less positive reactions than the other forms of schizophrenia (20.9 %:34.7 %). As already pointed out, this naturally depends also on the question whether the diagnosis of catatonia is more or less accurate. The difference found by us to the advantage of the other forms of schizophrenia is, however, so great that also by a less accurate diagnosis "catatonia" it can with difficulty be said that the catatonics give more positive reactions than the other forms.
- (3) Indeed, women show more positive reactions than men, but in the first place this is not only the case with the schizophrenics (35.7 %:28.1 %) but also with the control group (32.8 %:29.3 %, including the normals 36.6 %:29.3 %). On the other hand this difference is not nearly so great as that found by *de Jong* and *St. John*.

In internal medicine an extensive literature about this reaction of *Hanger* has been published. It has been shown that the technique has a great influence on the results. The reaction is photosensitive and the tubes in which the reaction takes place must be kept in the dark. Also the newly made antigen solution has to be mixed with the serum very soon.

Considering my figures and taking into account that there is apparently no difference in result between the group of the schizophrenics and the control group it may be concluded that evidently 526 individuals without liver damage showed 172 positive reactions, that is 32.7 % on an average.

Whence this great number of positive reactions? In my investigations I used the originally described technique (see p. 139) and took care of preservation in the dark and of the speedy usage of the fresh antigen solution in order to compare my results with those of *de Jong* and *St. John*.

It has been shown by the different experiments with the *Hanger* test, that this technique with aqua dest. of 70° C. gave

a too sensitive solution, through which too many positive reactions arose. Therefore a modification in which the antigen is mixed in the cold with the aqua dest., and afterwards heated is now used. Therefore I have repeated my examination with the modification of the test. For the results see Table III:

TABLE III
Modification of test.

Diagnosis	Number of Cases			Pos. reactions			Percentage of		
	m	w	T	m	w	T	m	w	T
<i>Schizophrenia</i>									
Catatonic	32	16	48	1	2	3			6,9
non-catatonic	87	123	210	5	13	18			8,6
	119	139	258	6	15	21	5,0	10,9	8,1
<i>Control-group</i>	m	w	T	m	w	T	m	w	T
epilepsia	7	6	13						
man-depr. group	16	28	44	2	2	4			
dem. sen. et art.	21	14	35	1	1	2			
oligophrenia	29	41	40	3	5	8			
other psychoses	18	18	36	1		1			
	91	107	198	7	8	15	7,6	7,5	7,6

The modification is, indeed, far less sensible than the originally described test, but again there is no difference between schizophrenia and control-group (8.1 %: 7.6 %), nor between catatonia and the other forms of schizophrenia (6.9 %: 8.6 %).

For the rest opinions in internal medicine about the reaction are still greatly divided. While from the American point of view a certain value is attributed to the reaction, on the other hand there are also contrary opinions. In an extensive Swiss study (3) the point of view has been taken, that the reaction—non-specific—would have nothing to do with liver ailments.

However this may be, for psychiatry it probably will not be of that significance of which *de Jong* and *St. John* imagined it to be.

SUMMARY

The author examined 261 schizophrenics and 265 control cases (other psychoses and normal individuals) with the cephalin-cholesterol flocculation test of *Hanger*. In contrast to a previous examination made by *de Jong* and *St. John* no differences were found between schizophrenics and control cases and even less positive reactions with the catatonics than with the other forms of schizophrenia. In the case of women more positive reactions were found, both with schizophrenics and the control group, than with men. This difference, however, was rather small.

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NEED OF A GENERAL PSYCHOLOGICAL THEORY COMMON TO NEURO-PSYCHIATRY, PSYCHOLOGY AND THE SOCIAL SCIENCES

Introduction to a series of biopsychological studies.

BY

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Karl Bühler in "Die Krise der Psychologie":
Es ist, wenn nicht alles täuscht, keine Zerfalls-,
sondern eine Aufbaukrise, ein embarras de ri-
chesse, wie er das Ausholen zu einem umfas-
senden Gemeinschaftswerke begleiten kann. Ge-
lingt es, eine Konkordanz herzustellen, dann
dürfen wir Grosses von der Zukunft erwarten.
Kritisch ist ja nicht nur die Lage in der Psycho-
logie, sondern auch die in anderen Geisteswis-
senschaften und in der Biologie: ich denke mir,
unsere nächsten Nachbarn, z. B. die Soziologen
und die Psychiater, dürften nicht nur aus al-
truistischen Gründen an dem, was uns hier be-
schäftigen soll, Interesse nehmen.

Previously psychiatrists not infrequently showed a depreciatory, or even slightly hostile, attitude towards psychology. Presumably this was due to the fact that the psychologists then did not have very much information of value to offer psychiatry. Besides, either branch of science spoke its own language—and, unfortunately, they still do. This is the more regrettable as during the last score of years psychology has developed so much that now it really has something to offer to psychiatry. Today a psychiatrist without psychological knowledge is in the same situation as that in which an internist without physiological

knowledge would be. Psychology has simply become a section of physiology—and at that, a very important section.

The matter is quite parallel with the relation between psychiatry and neurology. This subject has often been discussed—sometimes very ardently. As far as can be seen, the signal point is that it is important *clinically* to differentiate between these two branches of science, while it is equally important *scientifically* to consider them together; and if this unity scientifically fails to be recognized, also these two closely related sciences will each speak their own tongues.

This, among other things, implies that a fundamental psychological theory must apply to the conceptions of neurology as well as to those of psychiatry—nay, it will have to be adjusted also to the principles of experimental psychology, philosophy, philology, ethnology, pedagogics, sociology, criminology, etc., in other words, all the branches of science dealing with the mind. It would be of immense importance if these branches of learning spoke the same language and worked with the same fundamental psychological concepts. Then the way would be paved for a profitable collaboration instead of the present conditions: each profession being enwrapped in its own system of conceptions and specific terminology.

Obviously such a comprehensive and fundamental psychological theory should apply to animal psychology as well as to child psychology and adult psychology. Correspondingly it will also have to be in keeping both with child psychiatry and adult psychiatry. It will here be appropriate to emphasize at once that *if* adult psychiatry in the daily clinical work may be taken care of by psychiatrists without special psychological knowledge, this will not hold true of child psychiatry, in which all too many threads are interwoven with those of general psychology and where the routine collaboration with school psychologists and kindergarten teachers quite naturally requires a considerable overlapping of knowledge. Moreover, this is absolutely required for any scientific work in this field. It is not only desirable but also necessary that child psychiatry should be placed on a solid foundation in psychology rather than grow out as a branch

on the structure of classical psychiatry. Among other things, this requirement has developed from the large number of cases of social maladjustment in relation to the cases of psychosis proper, which indeed are rare in childhood.

What has been emphasized here concerning child psychiatry also applies to the other daughter specialities within the domain of psychiatry: forensic psychiatry, military psychiatry, industrial psychiatry and social psychiatry. Here we might mention also the topical problems of psychopathy, which, as far as may now be judged, can be solved only through a joint psychological-psychiatric dealing with the problems. In this field *Kinberg* has pointed out the way in an exemplary manner. Finally, it should be kept in mind that a steadily increasing field for psychiatric work is made up of the neuroses and the psychotherapy—and, I think, nobody will question the significance of psychology to the understanding of the neuroses. When attention is called to the role of psychology just now, it is because psychiatry in many respects is about to make a change in signals. In the Scandinavian countries the classical German psychiatry with all its complicated terminology is about to retreat to the background in favour of the simpler and clearer Anglo-Saxon psychiatry. Furthermore, *Essen-Möller*, *Strömgren* and others commenced working for the elaboration of a clearer terminology and more modern diagnostic tables. These efforts are followed with interest by many colleagues to whom the classical psychiatric terminology seems inconvenient. The present paper is to be taken as a contribution in the same direction. Its purpose has been to point out the importance of a coordination of the future psychiatric terminology with modern psychological views.

Various Schools within the Field of Psychology.

One thing must be said in some degree to excuse the wanting respect of psychiatrists for the science of psychology, namely: its hitherto pronounced split-up into different schools. In trying to find a psychological answer to some concrete psychiatric question it often turns out that psychology offers not one but

several answers, representing various schools within this science. It will be appropriate, therefore, briefly to look into these different schools of psychology.

In the first place we meet with the classical *association psychology*, which was elaborated especially by *Ebbinghaus*. Further, the *Pavlov-Bechterew reflexology*, which again gave rise to *Watson's behaviourism* and *Thorndike's trial-and-error theory*. About simultaneously with the advancement of reflexology, *Freud* elaborated his *psychoanalysis*, and *Adler* his *individual psychology*, both of which introduced valuable dynamic approaches to fundamental psychological problems. Related dynamic points of view were vividly developed by *Janet*, who attached particular importance to an energy-economical conception of "la force neurale". A similar temperamental dynamist was *McDougall*, who in his "hormic" psychology, among other things, arrived at the result that the "neural force" consisted in a hormone-like substance, which he termed "neurin". His prolific and markedly introspective considerations were greatly influenced by *William James's "common sense psychology"*, which early and clearly had drawn the line at the classical German orthodoxy. Finally, mention is to be made of the more recent German schools: the *Semon-Bleuler mnemonic theory*, *Kretschmer's medical psychology* and the *gestaltism* as elaborated by *Wertheimer*, *Koffka* and *Köhler*, with *Rubin*, *Katz* and *Lashley* as liberal free lances.

A more comprehensive and also more complicated survey of all the different schools in psychology has been presented by *Müller-Freienfels* in this form:

Preponderantly objectivistic theories.

1. Association psychology: *Ziehen, Ebbinghaus, G. E. Müller.*
2. Voluntaristic apperception: *Wundt.*
3. Classifying intentionalism: *Brentano.*
4. Sensory-motor actionism: *Wm. James, Lange, Münsterberg.*
5. Eidetics: *Jaensch.*
6. Ideology: *Külpe.*

7. Gestaltism: *Wertheimer, Koffka, Köhler.*
8. Psychoreflexology and behaviourism: *Pavlov, Bechterew, Thorndike, Watson, Dewey.*
9. Parallelism and dualism: *Semon, Hartmann, Driesch, Bergson.*

Preponderantly subjectivistic theories.

1. Actional or functional psychology and phenomenology: *Lipp.*
2. Personalism: *Stern.*
3. "Lebenspsychologie": *Groos, Müller-Freienfels, McDougall.*
4. Psychoanalysis: *Breuer, Freud, Adler, Jung, Bjerre.*
5. Individual psychology: *Adler.*
6. Medical psychology: *Kretschmer, Jaspers.*
7. Characterology: *Klages.*
8. Cultural psychology: *Dilthey, Spranger.*

From this it will be obvious that when for some reason or other we call on the psychologists we meet with a highly variegated picture due to the great number of rivalling schools. As far as can be seen the main cause of this unfortunate state is to be found in the

Autism of the Leading Psychological Investigators.

This headline refers to the fact that the founder of a new theory—the head of a new school—is occupied so strongly with his own points of view that they are incorporated as dynamic parts of his personality, with a tendency to expand beyond the given borders. Here his desire for self-assertion sets in, demanding that others must recognize the results that have cost him many years of work, perhaps all his life. As these investigators generally are vivid and highly intelligent persons, with a pronounced faculty for a general survey, they are often excellent pedagogues with an eminent capacity for suggestion of their fellow-men through the spoken word as well as through their writings.

It is easy to understand that a thinker who first finds an

apparently reasonable connection which other investigators have failed to notice, must experience a strong emotional reaction in connection with his observation. Indeed, this is quite on a line with the mystic experiences known from the revelations and "religious revivals", in which the tendency to be filled entirely with the given message and the strong desire to preach it for the whole world is evident. When scientists fall for such a cataclysmic reaction it will often lead on to unjustified expansion of the validity of the laws discovered and a tendency to quick discarding of other views.

Naturally this tendency occurs not only in psychologists. It is familiar to practically all research workers, who by themselves try to master it as far as possible. But most natural sciences work with such a high degree of exactness that erroneous theories will soon be revealed, and hence the delay and confusion in the development of the respective sciences will be limited. It is a different story when something of this kind happens in the less exact sciences as, for instance, philological and historical research, ethnology, sociology, psychology, and psychiatry. Any investigator who has made a great achievement in these fields, may, so to speak, dominate the picture and for considerable length of time make the entire flock follow him wherever it suits him to go. The science will thus have to develop in a cumbersome zig-zag course with frequent regressions, almost like a football in a game. In these branches of science too many efforts are wasted in debating various questions. For even though the controversies sometimes may bring forth a new and valuable point of view, unfortunately the general rule is—just as in war and politics—that both parts leave the battle field even more embittered against the counterpart than before meeting and even more sure of themselves being right.

But, cannot this state of things be remedied?—Fortunately and decidedly: Yes! For, a new mentality has already begun to grow up, one of the most important remedies here being a reduction in the stubborn cult of the *priority claim*. Recently, in a little book, highly worth reading, entitled "The Examination of Reflexes—a Simplification", *Wartenberg* made a fairly thorough

clean-up in the field of neurology. He primarily wages his war against the many investigators who by their "clamors for priority" have tried to find "an open backdoor to immortality" by discovering some new, more or less subtle, ways of eliciting the various reflexes already known (quoted from the preface by *Foster Kennedy*); as a result of this tendency, neurology has become very difficult to master because one would have to know the name of all these innumerable "reflexes"—which contributed greatly to scare the students away from the neurological textbooks, and thus to isolate this branch of medicine too much. Wartenberg is fully aware of the psychological factors that led to this development. Thus he says: "The history of reflexes provides an interesting chapter in the book of human vanity—a chapter often not lacking in tragicomic elements," and he reminds of the old word: "There is nothing new save that which has been forgotten." He concludes his book with the following passage, which stimulates to reflection: "Modern neurology needs and wants more physiologic orientation. Every new observation in clinical neurology should be subjected to a strict physiologic interpretation."—It is to be hoped that books of this sort will appear also in psychiatry and psychology.

As to this "clamor for priority," it is a pleasure to be able to establish that the Anglo-Saxons always have shown a gentlemanlike control of the tendency to extol their own glorious achievements, whereas such broadcast self-appraisal has always been a conspicuous continental character. It is also a characteristic feature, indeed, that the modern *team-work* originated in the Western countries. On the British and American sports fields the young are educated to play together and work together; no single player gets all the glory—it belongs to the team. A similar fellowship in scientific work has proved a very poor soil for autism, and thus the tendency to extreme generalization is avoided to a great extent. Undoubtedly, in no slight degree this is due to the fact that the team covers a far greater material of experiences than does the individual investigator; and the greater the knowledge, the lesser is the risk of autistic conclusions. Therefore, it would mean an important advance if

team-work made headway in the less exact sciences. Just imagine the benefit that would be derived from great "interdepartmental teams," comprising neurologists, psychiatrists and psychologists to establish a terminology for all common subjects—let alone the benefit such team-work would mean to all the social sciences (sociology, ethnology, philology, school psychology, pedagogics etc.).

Still, not all kinds of research require team-work, and even without team-work it is possible to limit the tendency to autism. Here I have in mind the *form* in which the investigator presents those parts of his work that are in conflict with previously accepted views and with theories advanced by other authors. Often we meet with a quite unnecessarily sarcastic form, stamped by an undisguised fighting spirit (*Huizinga's* "agonal attitude"). It is difficult to see why one should not always be able to advance one's opinion about a problem with full recognition of the scientific spirit in the views of other investigators. The opposite attitude does no good to anybody—least of all to science. Even when the opponent is lacking in faculty, in spite of his good intention, there is no reason to judge him too harshly, for the lesser and plodding workers are justified as well as are the great soaring eagles—indeed, most of us belong to the former category. There would even be some reason for asking at what level all sciences would be today if we had not got the many small investigators. Science is highly in need of diligent bee workers, and naturally they are entitled to be treated decently. Science is such a noble game that it should be played according to gentleman rules—from which the play will benefit. In his latest book, *Cannon* aptly says: "The investigator should be generous to his fellow scientists!"

Yet, autism is merely one of the factors which have drawn inevitable border lines. Another obstacle is found in the

National Antagonisms.

Russell has suggested that "all animals that have been carefully observed have behaved so as to confirm the philosophy in

which the observer believed before his observations began. Nay, more, they have all displayed the national characteristics of the observer. Animals studied by Americans rush about frantically, with an incredible display of hustle and pep, and at last achieve the desired result by chance. Animals observed by Germans sit still and think, and at last evolve the solution out of their inner consciousness."

Still, this joking characterization contains a large grain of truth. For illustration of such national contrasts it will be appropriate to cite what *Frolov*, the pupil of *Parlov* says about *Köhler's* chimpanzee experiment in Teneriffe: "Hence what *Köhler* is inclined to call the invention of an instrument of labour seems to be more the result of his ardent desire to discover what he, as a professor of psychology belonging to the theological faculty of Berlin University, has to discourse on from his professorial chair, i.e., the origin of abstract ideas. In *Köhler's* experiments we cannot help being disturbed by the excessive haste in drawing conclusions, and also by the almost complete absence of statistical data such as we are accustomed to see in *Pavlov's* experiments."

This is merely a single little heave from the larger storm between Russian reflexology and German gestaltism, which was one of the most senseless conflicts ever waged in the field of psychology. For while either school thought it had found the key to the mysteries of the mind, they really supplemented each other brilliantly, and a solid reconciliation on a rational basis would be one of the most fertile foundations for future psychological research.

As an example of the attacks made by the Gestalt psychology on the American reflexology we may take a short quotation from the gestaltic *Koffka's* characterization of *Watson's* behaviourism: "Learning could not be more completely reduced to mechanical terms. Even the question how the selection among different ways of response is to become effective, and what factor gradually determines the elimination of the useless movements, *have been answered by Watson in the simplest, but also in the crudest, and, as regards a natural feeling for living creatures, in the most*

unsympathetic manner." Such is the tone employed in dealing with Watson. As to *Thorndike*, who evidently is taken not to be quite so bad, Koffka feels that he can even afford to give him a little friendly-vitalistic slap on the back saying: "At any rate, he (*i.e.* Thorndike) considers the ethical aspects of development."

In the course of time many other rivalling theories within the field of psychology have shown a similar tendency to grouping according to national boundaries and thus give a reflexion of the general competition of the nations. In this connection it would almost be justified to speak of a *national autism*.

It is not in all places, however, that the soil has been favourable for such an attitude. Thus, for instance, in Switzerland, Holland, the Scandinavian and Anglo-Saxon countries a "freedom of confession" has prevailed for a good many years, with hospitable reception of new theories together with the local points of view.

Crossing the national border lines there is a sharp divide on an even more emotional basis, namely:

"Mechanism" or "Vitalism".

The difficulties involved in this problem have strongly inhibited the free development of psychology ever since the dark Middle Ages, primarily because they are closely connected with the temperament and view of life of the individual investigators. Probably in no other science has the personal view of life of the investigators played a greater role than in psychology (except in philosophy).

The signal point in the old controversy is that the mechanists advocate an entirely physico-chemical explanation of the mind and all its manifestations, whereas the vitalists believe that, besides the physico-chemical principles there exists some *specific psychic principle*— "life force," "nervous force," "living principle," "guiding force," and what not—that follows its own laws and is not definable as a reflex phenomenon or any other physiological reaction. Some vitalists even go as far as to claim

that this "psychic force" may persist independently of the cells—that is, they live in the no-man's-land of *parapsychology*.

While some psychologists, e.g. *Parlor*, *Thorndike*, and *Watson* stand clearly on the mechanistic wing, and *Bleuler* with his mnemonic theory occupies an isolated intermediate stand, we find *McDougall* on the extreme vitalistic wing, even with one leg in the bog of parapsychology. Thus, among other things, McDougall maintains the theory that the integration in the concentration of attention and in voluntary acts takes place through *telepathy* between the various sections of the nervous system. His argument is as follows: When the phenomenon of telepathy has been proved (as he reckons it to have been) and is found able to coordinate the minds of two persons, what will it not be able to accomplish within the central nervous system of the individual person? — It is not to be wondered at that the mechanists take this argument to be wide of the issue in question. Here it should be kept in mind that McDougall is a gifted and highly estimated investigator who has had great influence on the development of psychology. *Parlor* says plainly: "Some investigators cannot do without the faith of their childhood." And *Freud* states that "one has to be strong in order to carry a certain load of uncertainty."

At present matters may be said to stand so that the alternatives of "mechanism" and "vitalism" each designate a *cherished wish* of the two groups of investigators. They wish that the whole thing may be explained on a physio-chemical basis, or that everything takes place under the guidance of a governing force.—But the solution of this problem is hardly practicable yet, as we have not yet advanced beyond the very beginning. For a good many years we shall have plenty of work in gathering facts and grouping them under common viewpoints. Then time will show who are right, the "mechanists" or the "vitalists"—or neither.

Besides the various forms of *subjectivism* mentioned already, there is still another very important one, namely:

“Animism”.

Although animism is by no means a modern concept, only in recent years it has been realized how strong a factor it is in all forms of research (*Ogden, Richards, Chase, Hayakawa, Segerstedt, Agerberg and Anders Olson*). This term is mostly familiar from its connection with primitive peoples, as spiritualization, indeed, is the fundamental feature of any primitive mind. When a little girl plays with her doll, she believes that it feels and acts just as she does herself; when primitive man sees a tree, he assigns to it a soul like his own. When we study the mind of the animal we are inclined to interpret it in a more or less human fashion (anthropomorphism). Similarly, in studying the minds of children, we are inclined to look upon them as small adults. When the modern European considers the native races he likewise attributes to them a more or less European mind (*Vilh. Grønbech*). So, in all such cases there is a scientifically dangerous application of the individual's own mind to the surroundings—as a part of a general “anthropocentric” tendency.

It is obvious that in the field of psychology the “subjectivistic” schools run the same risk of misinterpreting the psychic reactions in keeping with the introspective experiences of their own “private” mind. Furthermore, there is a risk of “personification” of various psychic conditions—*e.g.* “consciousness”, “sub-consciousness.” “das Es,” “das Ich,” “das Über-Ich”—so that these elements are interpreted as independent agencies that “act,” “make efforts,” “counteract each other.”—Not only the things, indeed, but also the concepts and words have their animistic force—the magic of words (*Segerstedt*).

Returning to the children, in whom everything is more simple and transparent, at a certain stage we find the word almost to be identical with the thing, so that here, correspondingly, the word has the same animistic validity as the thing. The little girl will say: “Yes, father, but there must be a God—for he has got a name.” To the child the idea of God applies so strongly to the name, that this quite naturally is used as an

argument in favour of the existence of God.—*The very same thing is met with in science*—as was pointed out already by *Hughlings-Jackson*. He never tired of telling about the old woman who rejoiced in Adam and Eve having been fortunate enough to name the animals just correctly. Also *Agerberg* tells an English anecdote about a horse being called “cheval” in French, “hest” in Danish, but “horse” in English—“and that is what it is.”

It is this *validity of the words per se* which largely is to be blamed for the slow development of science. Unprejudiced investigators may point out the shortcomings of the prevailing concepts, but hitherto they have but seldom succeeded in eradicating the old concepts and trends of thought before the contemporary scientists have died and a new generation grown up. In the past century this sort of exchange required several generations—but, then, this was indeed the golden age of the “terminologists”. Fortunately the tendency of this epoch to unnecessary definition and description produced a certain irritation in a number of unprejudiced investigators, so that the expansion of the terminologists was limited to a certain extent. Thus *William James* once said that rather than read the endless chapters on the emotions of the mind as elaborated by the classical psychologists, he would prefer to study a description of the shapes of the rocks in New Hampshire.—In the same spirit, *Karl G. Lawin*, the Swedish historian of art, is said to have stated emphatically that rather than read any fairly large German history of art he preferred again to be afflicted with gravel in the kidneys.

Nevertheless, as a matter of fact, sciences such as psychology, psychiatry, and neurology are still dragging around with an enormous armamentarium of terms that makes them difficult to learn and impossible to survey. Here the terminology means a burden rather than a facility of orientation—something which highly contributes to scare the young students from entering into these sciences. For this reason, too, we undoubtedly should make use of the present favourable time for the introduction of English as the choice language for scientific work,

as English is one of the languages least encumbered with professional terms of a more or less animistic nature.

CONCLUSION

What is needed in psychology today is not new schools but simplification and reconciliation of the present ones. This might perhaps be attained through large-scale cooperation between psychology and neighbouring sciences—a sort of psychological U.N.—with appertaining clean-out of all undesirable subjectivistic concepts and terms (*e.g.*, “autistic,” “nationalistic,” “confessional,” “animistic” and “anthropocentric”). In this way it should be possible gradually to build up a clear and substantial working theory that might serve as the common foundation for future scientific work within the many fields grouping round psychology.

SUMMARY

It is pointed out that important sciences such as psychiatry, neurology, and the “social sciences”—*e.g.*, pedagogics, philology, ethnology, sociology, criminology, philosophy—are more or less closely connected with psychology. So, for practical reasons, there is a strong need of a modern psychological basic theory which, besides being a support for each of the sciences mentioned, might help to bring the various sciences on better speaking terms than is now the case.

At present we find psychology divided into different “schools,” each of which on the basis of its particular experiences has formulated a programme which it tries more or less eagerly to get recognized as applying to the mind in general. In many cases the distinction between these schools is unnecessarily sharp.

Trying to find the reasons for this state of psychology, we have pointed out the tendency to “autism” in several “heads of the school”. We have seen how this scientific autism was more pronounced in countries where the *personal priority* was cultivated preferably, while it receded to the background in countries where *team-work* was the most common form of work.

Sometimes this autistic tendency proved to be accentuated by national aspirations to the leadership in the field of psychology, so that it is justified to speak of a sort of "*national autism*".

Another reason was found in the *confession-like controversy* between the "mechanistic" and the "vitalistic" conceptions, which have left their heavy stamp on the development of psychology. These two alternatives are to be looked upon as cherished wishes of temperamental investigators. But, presumably, it is all too early yet to take any definite stand concerning these theories because we still know too little for such a decision.

After this, it was mentioned how "*animism*" has imbued the mind—the scientific mind not excepted. The main reason was found in the *magic force of the word*—a phenomenon that has always muddled science and delayed the spreading of new productive ideas. It is emphasized how certain epochs and certain nations have been particularly given to this cult of words and concepts, so that the cathedra not infrequently would replace the laboratory. So, for this reason, too, we should try to use the present world situation to make English the official language of science because it is least encumbered with animistic terms.

ADDENDUM

The direct occasion for the appearance of this paper is "The International Congress of Mental Health," which will meet in London in August 1948. The main subjects to be dealt with by this congress are child psychiatry, psychotherapy and mental hygiene. The congress will be arranged according to partly new principles, as psychiatrists, psychologists, antropologists, and pedagogues will be present at the meeting. Efforts are being made to introduce an intense collaboration notwithstanding the national frontiers and interdisciplinary obstacles. On this account, stress will be laid on group-work rather than on individual achievement.

During the war these principles were so productive that it is planned now to adjust them to the work in times of peace. Particular importance will be attached to the aim of making this

new working form familiar to those countries that during the war had no opportunity to try out its advantages in practice.

With a view to the high aims of the congress, its preparation has been going on very thoroughly for over one year, and working groups—mostly “interdisciplinary groups”—have been formed in several countries to break the ground for the congressional transactions and constitute the germ of the future cooperation which, we hope, will be the most important result of the congress.

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PSEUDOPARALYTIC ACUTE CONCUSSION PSYCHOSIS

BY

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The rare occurrence of the pseudoparalytic concussion psychosis may perhaps justify us in reporting a case of this disorder, at the same time calling attention to the existence of this form of psychosis. The Scandinavian literature has not included any great number of publications on psychoses that have been the direct outcome of *commotio cerebri*, which, however, must doubtless be considered due to the fact that these psychoses are of rare occurrence in Scandinavia. In 1942 *J. Cedermarck*, Sweden, published a statistical statement of the course, symptomatology, and prognosis of 1,963 cases of cranio-cerebral lesions and found only 0.3 per cent. classifiable as "episodical psychoses," but no regular concussion psychoses were included in the material. In 1937 *Malzberg*, on the other hand, pointed out that from 1910 to 1935 the State of New York had a gradual increase in the number of cases of traumatic psychosis "from 2.1 per 1,000,000 general population in 1910 to 9.5 in 1935."

Some psychiatrists have, incidentally, been somewhat uncertain and reluctant to recognize the acute concussion psychosis as a nosological entity, so that as late as 1944 *N. Moros* would not venture to go in for the concept of acute concussion psychosis, but modestly suggested "psychosis undifferentiated with traumatic factor." But it seems to us that one remains on neutral clinical ground when employing the criteria established

by *Aug. Wimmer* for a concussion psychosis: (1) The trauma must have hit the skull, (2) the trauma must have been of a certain intensity, (3) there must be a certain relation in time between the trauma and the ensuing psychotic symptoms, (4) the traumatic mental disorders must manifest themselves in the form of an exogenous reaction type.

Consequently, when these 4 requirements are satisfied in a case, it seems to us to be most natural to use and maintain the term concussion psychosis.

The special type of concussion psychosis that has been termed the pseudoparalytic form was rather early described by French psychiatrists, and *Dupont & Courtois* are absolutely right in stating that, actually, it is only the humoral system that may allow us to establish the diagnosis of pseudoparalytic acute concussion psychosis, for this form of psychosis practically covers the clinical picture seen in acute paralytic dementia. In 1939 *P. Eichler* reported 3 cases which he termed "traumatische pseudoparalyse" and he believes there is every reason to maintain this diagnosis.

During recent years the traumatic pseudoparalysis has been discussed in a decreasing degree, for reasons we do not understand, these cases having been classified as concussion psychoses with expansive syndrome.

Most authors have chiefly followed the descriptive lines laid down by *Kalberlah* already in 1904, when he described the three stages or phases passed by an acute concussion psychosis and in particular the acute concussion psychosis with the amnesic-confabulatory syndrome (*Korsakow*):

- (1) The initial loss of consciousness—coma lasting from hours to days.
- (2) The delirious, transition stage of some days' duration, also with hallucinations, sometimes with a certain stupor or apathy, but in most cases with imperative motor unrest.
- (3) When the phase of motor unrest has passed away, the amnesic stage with the *Korsakow*-syndrome now appears, frequently accompanied by affective disturbances lasting

from weeks to several months, most frequently ending in paralysis.

Some authors, in particular *G. Zillig*, have shown that stage (2) may take a somewhat different course, as *Zillig* reported a case in which that stage could be divided into two well-defined phases:

- (a) Delirium with disturbance of consciousness and great motor unrest; the disturbance of consciousness is rather massive with confusion and difficulty of perception.
- (b) The next phase displays a change of consciousness that is not particularly conspicuous, but here the expansive confabulatory clinical picture is seen, and, in some cases, there are peculiar linguistic disturbances.

The disturbance of consciousness here is said to be of another nature than in phase (a), being rather of the nature of a "reinen Dämmerzustand," but it seems to be able to appear as rapidly as it disappears; thus it is not constant, and in the case reported the blurring of the patient's consciousness increased in the evening but, strangely enough, the orientation as to place and time is not impaired in this state of consciousness, and any marked "Merkstörung" could not be demonstrated either. Whilst the patient is afflicted with the expansive syndrome he seems to deal with his accident in a manner suggesting some created and elaborated knowledge of the accident, but as soon as the expansive syndrome has abated there is again a complete amnesia as regards the accident.

The division of stage (2) into two well-defined sections cannot apparently be observed with certainty in *Eichler's* three cases of concussion psychosis "die, sowohl durch ihr psychisches Symptomenbild von der Art einer, ein Korsakowsches amnestisches Syndrom begleitenden, mehr oder weniger hochgradig manischen Affektstörung mit profuser, expansiver Wahnbildung, wie durch den neurologischen Befund von gekuppelten Pupillenstörungen und Hypo- bzw. Areflexion, eine bemerkenswerte besondere Typik zeigen"—for which reason he terms the case one of concussion psychosis with a pseudoparalytic picture—and, according to *Eichler*, predisposing endogenous or exogenous

bodily factors, in particular addiction to alcohol, are not necessary conditions of the occurrence of such concussion-psychotic states, but he supposes that it must depend upon the nature, the extent, and the seat of the traumatic lesion whether a commotio cerebri or a concussion psychosis occurs.

Courville, on the other hand, more precisely states that a subdural hematoma may be a contributory organic factor in the duration of a posttraumatic psychosis, and *Foster Kennedy*, too, draws attention to the chronic subdural hematoma which may "simulate psychoneurosis, amnesia and now and again display a Korsakow syndrome."

In contrast with *Eichler*, some authors have stated that chronic alcoholism must doubtless be included in the pathogenetic considerations of the occurrence of the expansive syndrome in the acute concussion psychosis.

The 9 cases of *Arnold F. Friedmann & Charles Brenner* thus included 7 patients who were chronic alcoholists, but they just stress the contrast between the course of these psychoses and that of the classical Korsakow psychosis (amnesic-confabulatory syndrome plus polyneuritis) in which the psychic disturbances persist for periods from 6 to 12 months or become chronic.

The following is a report of a case which we have had the opportunity to observe:

P. H. J.—aged 42 years.

Mental Hosp. Viborg (case book No. 9954).

Sept. 14th to Dec. 17th, 1946.

Predisposition: A maternal aunt oligophrenic. His father and his paternal grandmother suffer from diabetes mellitus.

The patient has always been limping a little because of a coxa vara dxt. (congenita?).

He has always been diligent and industrious—now being a workman, now an assistant waiter—always taking odd jobs. During recent years he has been running a second-hand business together with a brother of his; he has always liked trading and has a fairly good sense of appraising things.

Abus. spirituos.: About ten years ago the patient was a holiday relief at a brewery, but had to give up that work, as he had been drunk every day for a couple of weeks.

During the years that followed he only took spirits on festive occasions, but then he had another period of *abusus spirituos.* lasting all through the summer of 1945 and causing his family to make him join a temperance society in Dec. 1945 and since then the patient has drunk no spirits at all.

Accident: Having been run down by a motor-car on July 4th, 1946, the patient was admitted to the local county hospital in a state of unconsciousness, and remained unconscious for 4 days (on July 6th lumbar puncture was made, with removal of sanguinolent spinal fluid). During the days that followed he reacted, was, however, stuporous, but about the 18th July he became very talkative, twaddling, sometimes very restless, shouting and noisy and sometimes aggressive; he was frequently dirtying himself. This period of unrest lasted for 8 to 10 days, his faculty of retaining impressions was nil and, consequently, his wife had to play up to him, otherwise he became quite furious. He got the idea that a certain man owed him 2,000 Kroner for "a wardrobe full of clothes." Hoping to appease the patient, his wife then told him that that matter had been settled and that she had received the 2,000 Kroner. (Later, his wife learned that about 1½ hours before the accident the patient had just been seeing the man in question in order to offer him a second-hand tent at a value of about 100 Kroner, but the man did not want to buy the tent.)

Psychiatric examination on Aug. 1st, 1946:

Name in full: +.

Date and year of birth: +.

Present year: "I suppose it is something with 1900 again."

Age: "I am 36 years—yes—and I am quite well."

Month: December.

Can't you see the trees are green: "Well, then it is strange to speak of December—still, one has the feeling of approaching Christmas."

Why in hospital: "I have caught a diphtheria, as so often before."

Occupation: "I am a workman, but was also running a furniture shop together with my brother."

Memory: "Excellent."

Furniture shop: "It is running excellently—I have a turnover of at least 2,000 or 3,000 Kroner a month and this year I have had a profit of 1,000 Kroner monthly.

He told that the other day he went to see his family in Vestergade (the street where the patient lives is Adelgade) just opposite; he thought then that the younger children were not so glad of his presence. He believed that the younger children ought to be infected with diphtheria in order thus to acquire an increased resistance.

He stated that he had 18 children "but had hardly got the names of

all of them"—believed that his wife had rented a flat at 13, Adelgade (the patient's residence for several years), but hardly knew where that street was in the town, he supposed the flat had 4 rooms. He had been married to his wife for 30 years, this year he was christened by Dr. S., the senior physician (of the county hospital), but could not understand why he had been accused of being 86 years. Later he stated that he and his wife had 30 children and that 18 of the children were christened the other day at the same time.

He was extremely fit, highly satisfied, kindly disposed while being examined—markedly euphoric.

Neurological examination: Right pupil slightly irregular, reacting sluggishly to light.

Fundus natural.

No disturbance of speech.

Upper extremities: Slight preponderance of reflexes on right side.

Lower extremities: Slight preponderance of reflexes on left side, with an approach to ankle clonus. Plantar reflexes uncharacteristic; on the right side, however, rather of the Babinski type.

His grotesque confabulation remained unchanged, as did the vague expansive ideas and the euphoria, but the unrest abated and in a fortnight his orientation as to time and place improved.

On Sept. 14th, 1946, 78 days after the accident he was transferred to the Mental Hospital at Viborg. He was orientated as to time and place, was talking much, eagerly demonstrating, gesticulating, telling that he was coming from the isolation department, where he had been owing to diphtheria. He had "infected" many people, in particular many children, with diphtheria—a kind of vaccination; he said that in this manner he had become known all over the town, he had "infected" almost everybody, first and foremost his own children, about 25, that is to say 5 of them were his own children, the others were only his foster-children; still, they were not boarded with him, but were living with their respective parents. They had become his foster-children because their parents had applied to him in order to get the children christened, as he knew far better; he knew where to apply and where to get the different documents and so on. He had thus seen to the christening of many children in the town, had been christened himself many times, which was the reason why there was so much disagreement about his age. The clergyman said he was 86 years, he believed himself that he was 36 years, though he knew well enough that in reality he was 42. His wife was thirty odd years, they had been married for 35 years and he was to be married soon for the second time though they had not been divorced.

At the Mental Hospital he mistook the examining physician for a grocer. He reproached the night-nurse with being idle.

He did not recognize the doctor who examined him on Aug. 1st, nor did he remember the examination.

He was extremely fit—"splendid"—"excellent"—"certainly"—"don't you think so"—euphoric.

Sept. 16th: Did not remember his wife's age—"I have been married to her for many years—but we are to be married again on Nov. 28th—we will present ourselves at church in the ordinary way—we have been married several times previously in the same manner—this year I should have married two other ladies—but I withdrew and they did not take offence.—He and his wife have 4 children (+)—but for some time we had at least 16 foster-children—I thought they were going to stay in our home but they do not—but that happened this summer while I was not much at home.—Had he been travelling?—"No, it was because of the accident and diphtheria"—diphtheria transferred directly to him at his own request—the same had happened to all the children at home, including the twelve.

Was he in high spirits?—Indeed—and he was well off, too.

Yearly income? "12,000 Kroner—and that is not too high an estimate.—While we have been married I have never had to be close-fisted, we have had plenty of money for travels, entertainments, clothes and so on." He felt fine and was sure he could begin working to-morrow.

Letters to his wife and to a sister of his were correctly dated and marked "if undelivered, return to ..." in the right manner; he wrote that "what I have seen as yet here in Viborg is promising."

Sept. 20th: His faculty for retaining visual impressions was very poor—it was difficult for him to find his way in the department, he kept going to bed in the wrong beds and was equally astonished whenever he was corrected—told he was going to Viborg to-morrow, but did not mind staying here in Viborg—he was extremely indulgent, always admitting that his opponent was right, never being obstinate or arguing—otherwise his talk was all superlatives and he displayed the greatest subservience. Today he was 42 years himself—his wife was supposed to be 36—she had told him they had been married for 30 years—no doubt, they were to be married again.

Sept. 30th: His faculty for retaining was much better—he remembered the different visitors—"I have been told I was run down by a private car from Aalborg—stated to be on July 4th—thus on the Rebild Day—while I was in hospital I was under the impression all the while that I had not been run over—but it is true that I had diphtheria while I was in hospital—there were some who wanted to be infected by me, and this happened, too—and I am to be married again—that is true—and to the same wife—in spite of the fact that we have not been divorced, of course, or even thought of it—I have been married for 22 years and have 4 children—at one time my wife had taken a number of children

home to stay with her—later, I learned that they are not in our home, they just stayed a few days to be christened.

Oct. 11th: His memory had improved considerably—he had begun again to look at the newspapers, showed greater forethought—was somewhat solemn and supercorrect.

Nov. 1st: More collected, did not display expansive delusions any more, extremely unsuspecting and good-natured—was being taken advantage of by the other patients—but was highly satisfied with that—had never been pestering.

Nov. 28th: The patient's wife stated that he was pestering her to be discharged; he wanted to go home and do business, but the prices he mentioned as current in his line were quite imaginary.

A couple of times he reverted to the idea mentioned above, concerning an amount of 2,000 Kroner that was due to him—asked whether all the money had been spent—would know nothing of his wife's information—was then talking loud, whether she remembered 3 big square savings-boxes at home, brimful of money—when his wife said she had never seen those savings-boxes, he got very resentful. While she was there, he insisted on treating all those present in the department (35 persons) and also his mates (about 20 persons) to cakes.

Dec. 14th: His behaviour was quite unchanged—always exceedingly polite in hospital—slavishly compliant and content to be so, never making any objections or remonstrances, always thanking most respectfully and humbly, wanting to give the least possible trouble.

Today the following psychometric determinations were made:

(1) *Actual attention.*

(a) Sterzinger's test:

Only underlined two thirds of the letters normally underlined by healthy persons.

(b) Bourdon's test: was given up by the patient.

(2) *Intellectual attention.*

(a) "100-3 test"

solved by the patient in 90 seconds (normal time).

(b) The names of the months in reverse order:
spent 35 seconds (normal: 21 sec.).

(3) *Obligate faculty of retaining auditive impressions.*

Ranschburg's word-pair-method:

All pairs of words were remembered.

(4) *Faculty of retaining auditive impressions:*

Schultze's "10-word-test":

Number of readings ≥ 10 times (normal: 5 times at the utmost).

(5) *Faculty of retaining visual impressions:*

Recognition of 6 geometrical composed figures:

Recognizes 4 (normal minimum: 3).

(6) *Faculty of observation and perception:*

A "Storm-Petersen picture" is shown; 10 questions are asked, requiring at least 5 correct answers:

The patient gave 8 correct answers.

(7) *Course of associations.*

Enumeration of nouns for 3 minutes.

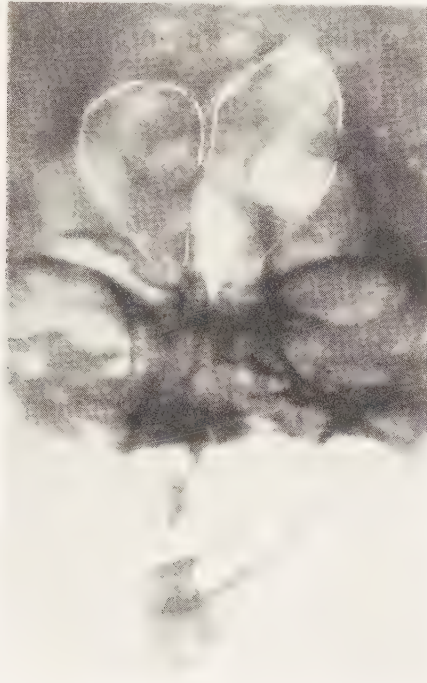


Fig. 1

The patient mentioned 42 words (manual workers at least 30 words).

(8) *Independent mental work.*

(a) Wippler's test (composing words of 6 given letters):

The patient formed 6 words (manual workers at least 9 words).

(b) Stransky's test (2 letters left out):

The patient managed 2 words (manual workers 5 words).

(c) Stating the difference between 8 pairs of abstracts:

The patient got 8 points (the normal being from 7 to 9 points).

(d) Inferring the moral from 10 proverbs:

The patient got 15 points (normal).

Arithmetical test: The patient did excellently.

Summary of psychometric determination: The actual attention was somewhat reduced, the intellectual attention normal, ordinary faculty of retaining auditive impressions poor, but the obligate faculty of auditive impressions was good; course of associations normal. Independent mental work slightly below the average, his skill in arithmetic slightly above the average.

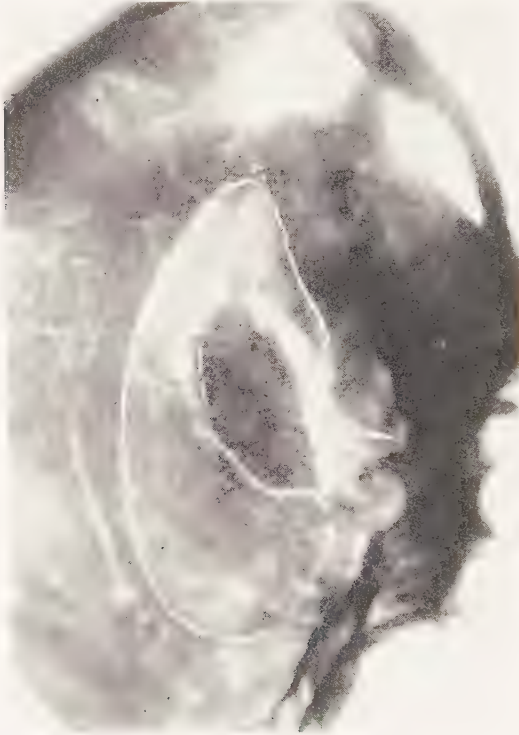


Fig. 2.

The patient thought the whole examination had passed off splendidly, excellently.

Examination of the eyes showed nothing abnormal now, apart from hypermetropia.

Dec. 9th, 1946: X-raying of the skull showed a rarefaction in the *left frontal region*, presumably due to a fissure. A similar rarefaction, though less distinct, was observed on the right side, and in roentgenograms taken in profile, quite a *distinct fracture line* was observed.

In encephalography, in which 70 cc. of spinal fluid were removed and

replaced by the corresponding quantity of air, the ventricular system was filled on either side. A very considerable dilatation of both lateral ventricles was observed, there was slight asymmetry, the left lateral ventricle appearing larger than the right, and there was some displacement to the right. The enlargement comprised the entire ventricle. The shape was, on the whole, natural. The outline of the gyri was very distinct and the sulci were broad, well over the thickness of a match. After half an hour, the gyri were still very distinctly outlined, but there was *no distinct flattening of the hemispheres. This picture is the sign of a considerable hydrocephalus int. and some atrophy of the cortex.*

Laboratory examinations: Hemoglobin: 94 per cent., sedimentation rate 3 mm., antistreptolysin titer 160. Leptospirosis test negative: urine, no abnormal constituents. Spinal fluid: Cells 18/3, glob. 0, alb. 10. Wassermann's test negative.

SUMMARY

The patient was a married second-hand dealer, aged 42, who had always been very diligent and industrious.

He has had two periods of *abusus spirituosorum*—the first 10 years ago, the second, one year ago lasting up to 6 months before the accident.

On July 4th, 1946, he was run down by a car—comatose for about 4 days. (X-ray taken on Dec. 9th, 1946, showed a rarefaction in the left frontal region, presumably due to a fissure. A similar rarefaction, though less distinct, was seen on the right side and X-ray taken in profile showed quite a distinct fracture line).

During the ten days that followed he reacted, was, however, distant—but on July 18th, 1946, marked motor unrest set on, he was shouting, noisy, confabulating, completely confused, his faculty of retaining impressions was nil, now and again both aggressive and dirtying himself.

This state lasted till about Aug. 1st, 1946, when he passed on to a phase of quiet euphoria, grotesque confabulation and expansive delusions. After the course of a few weeks his orientation as to time and place improved, but the psychic content was otherwise uninfluenced and his faculty of retaining impressions was very small.

His expansive and megalomaniac manner was without any real emotional background, and subsided gradually—while, at the same time, his memory improved—and disappeared completely about the middle of October, 1946.

Encephalography now revealed a considerable internal hydrocephalus, and psychometric determination showed the actual attention to be reduced, the ordinary faculty of retaining auditive impressions to be poor, independent mental work to be slightly below the normal, whereas the following functions were found to be normal: Intellectual attention, the obligate faculty of retaining auditive impressions, the faculty of retaining visual impressions, faculty of observation and perception, course of associations, skill in arithmetic.

He remained in a somewhat flat and idle frame of mind, frequently with a slightly euphoric touch, still dysphoria of short duration but often relapsing.

He has become more self-opinionated, more condemnatory, calmly absorbed in being so exemplary in all his doings that all his attention is spent on that purpose, his initiative thus only appearing sporadically.

The acute concussion psychosis he has passed through has thus left the patient with a considerably changed psychic structural formula.

Our case displays four interesting phenomena which will be discussed in more detail:

- (A) Elaboration in the course of the concussion psychosis of an episode that took place immediately before the accident.
 - (B) Disturbance of the patient's idea of time.
 - (C) Peculiar expansive ideas.
 - (D) The patient's elaboration of the accident itself.
-

re (A): About 1½ hours before he was injured in the accident, on July 4th, 1946, our patient had offered a tent at a value of

100 Kroner to somebody. About a fortnight later the patient was confabulating about the man in question owing him 2,000 Kroner for "a wardrobe full of clothes"—but to stop the patient talking about it, his wife told him that she had received the amount.

One day, about 4 months later, the patient repeated that an amount of 2,000 Kr. was due to him, getting excited because his wife would not supply him with ample pocket money during his stay in hospital.

The patient must thus have been able to remember what his wife had told him about the money, though it was otherwise noted clinically that his faculty of retaining impressions was suspended; for the patient further asked his wife whether she had spent all the money.

Now the patient did not want to accept his wife's explanation, however, but at once fabled and told her that surely she must remember the three big square savings-boxes they had at home, brimful of money. As his wife did not know of them either, the patient just dismissed the situation thus created by saying, "I am not an idiot, I am just as clever as the rest of you."

He left it at that and since then he has not been heard mentioning any claim for "2,000 Kroner for a wardrobe full of clothes" or anything about the "three big square savings-boxes brimful of money."

This is thus the case of an episode occurring immediately before the trauma of the skull and being elaborated in an expansive direction in the course of the second stage of the concussion psychosis.

In the course of the third stage of the concussion psychosis this expansive elaboration of the episode turned up a couple of times, caused by sudden excitement.

At the after-examination on Sept. 7th, 1947, the patient did not remember anything about it, but he told that "a bad lot" had owed him 2,000 Kroner during the last few years, the patient having financed that person's business to some extent.

He was unable to recollect anything of his speaking of the

three big savings-boxes that were brimful of money; but in his boyhood he was a frequent visitor to a house where they had three big savings-boxes, almost of the shape of a projectile, placed in one of the rooms.

re (B): The disturbance of the patient's idea of time was quite conspicuous during the first few months of his disease.

Van der Horst, for example, has pointed out that the disturbance of the estimation of time, "the tense mark," is the essential feature of *Korsakow's syndrome*.

The current view at present seems to be that lesions in the vicinity of the third ventricle give rise to disturbance of the perception of time and space and, in particular, of the placing of a certain incident in a larger sequence of time and space.

Anders Olson defines "time" as an abstraction for a definite kind of "internal milieu" occurring after a certain length of time (internal milieu = the sum of all the stimuli emanating from the reactions of the organism itself). "Time" is a necessary condition for a comprehension of space, and it must be supposed directly that the ideas of time must be very closely associated with intact functions of observation and memory. But, no doubt, *Strömgren* is right when, in his studies of disturbances of consciousness, he stated that time consciousness is hardly any independent quality of the function of consciousness, but simply forms part of the object consciousness. It is a well-known fact that some persons may go to sleep and wake up spontaneously at the time which the individual in question had decided on before falling asleep.

Since the chronological time notion of our patient had been suspended, he did not find it difficult to state that he had been married to his wife for 35 years and that he was only 36 years old himself (42). In 1935 *Ritchie Russel* drew attention to the peculiarity that patients with *commotio cerebri* or concussion psychoses are inclined to state their ages to be much lower than is actually the case. Later, *C. P. Symonds* was able in all essentials to confirm the observation made by *R. Russel*; although he was 42 years, our patient frequently stated that he

was 36—and our case is thus a small and modest corroboration of the observation made by *R. Russel* and *C. P. Symonds*.

There was no paraphasia or confabulation at all in this connection, for the patient maintained the ages he had stated for some time and promptly supplied them again when asked. On the other hand, he was astonished that he had been accused of being 86 years of age, but he readily eliminated that age through confabulation.

His remarks about having 30 children with his wife, about the 18 children having been christened "the other day" at the same time and his going to be married again to his wife "on November 28th," though they have never been separated, must doubtless be considered to be in keeping with the above.

At the after-examination on Sept. 7th, 1947, we learned that in the early summer of 1946 the patient's wife had been a godmother at two christenings at church; the patient did not believe, however, that these two events had actually had any great influence on him, but one cannot help thinking that they have supplied the raw material for an elaboration in an expansive direction during the concussion psychosis. It may be mentioned that during recent years—and in particular when their conversation or the situation was of a somewhat erotogenic stamp—the partners have used the following phrase, "do you want to be separated or do you want to be married," but in the course of the second stage of the concussion psychosis and during the first part of the third stage this phrase lost its emotional relation and the "joke" was by no means characterized by "Witzelsucht," but fell apart for him in two hard facts. The date frequently stated by the patient as the one on which he was going to start a second married life with his wife, is the actual anniversary of their wedding.

At the after-examination the patient could not with certainty refer to anybody who was 86 years of age, but his former landlord and landlady, with whom the patient is still having social intercourse, had in their house a grandfather, "a fine old man, his language was somewhat original;" once the patient's children had been playing in the staircase and had an-

noyed the said grandfather who then asked his grandson, a man about 10 years younger than the patient, to have the patient's children reprimanded. This was effected by the young man asking the patient to correct his children himself, a thing for which the patient admired the young man. Incidentally, it was this young man's brother to whom the patient offered a second-hand tent immediately before the trauma of the skull. The patient believes that the said grandfather died at the age of 86.

re (C): The patient's expansive ideas are not perhaps of formidable dimensions but still so unmistakable and given so determinedly and naturally as to cause us at once to think of dementia paralytica and, practically, one cannot by means of a single examination of a case of acute concussion psychosis with expansive syndrome clinically distinguish this picture from the acute onset of dementia paralytica. It seems to us by no means to be unwarranted to term this state "pseudo-paralytic concussion psychoses"—our patient believed to be 36 years, to have 30 children, had been married to his wife for 35 years, believed her to be 32 years, had 18 children christened "the other day," was famous for having infected all the small children of the town with diphtheria, thus rendering them "more resistant and well-behaved," was in excellent health and well-off—transiently extravagant—had been married several times, should have been married to 2 ladies this year but withdrew without causing any offence, etc. His frame of mind was not, however, perceptibly elevated and the patient did not show any great communicativeness, but the expansive tendency appeared soon after during a quiet conversation with the patient. The patient, however, was by no means of a particularly affective stamp in his intercourse and cooperation with the other patients, whereas his excitability became distinct when he was visited by his wife.

There is something incomprehensible in the expansive syndrome of concussion psychosis; as previously mentioned, it has been maintained that the concussion psychoses with the expansive-confabulatory syndrome were probably due to chronic

alcoholism, but, no doubt it cannot be said with certainty that our patient was actually suffering from chronic alcoholism but just that he has had two periods of *abusus alcoholici* and, consequently, the case cannot be classified, except for a clinical probability, among those in which it is believed that alcoholism may be a contributory factor in the development of the expansive syndrome of a concussion psychosis. But it may be stressed here that quite a large number of these forms of psychosis which could not be associated with addiction to alcohol have been communicated.

It is, however, peculiar that the expansive syndrome developed at the beginning of the second stage of the concussion psychosis and that, actually, nothing is added later on and, lastly, that, qualitatively, the expansive syndrome changes so little.

It seems to us, however, that our after-examination (including narco-analysis) was capable of revealing a series of pre-morbid events and episodes of an emotional stamp or determination which seem to be of great pathoplastic importance to the expansive syndrome of the concussion psychosis; it was found out, for instance, that 7 or 8 years ago the patient was frequently an extra waiter at a hotel where they had two "exceptionally nice, shapely, bright and charming waitresses," who had overwhelmed the patient completely and with whom he had been talking much, in particular after working hours. After about one year both girls left the town, and since then the patient has been out of touch with them.

It seems to us that this episode affords the material for the patient's recollection which he took out during the second stage of the concussion psychosis when he stated that this year he should have married two ladies, but had withdrawn "without offence."

During his psychosis the patient had a slight euphoria—rather a state of quiet satisfaction, he was all superlatives; as already mentioned, the expansive feature did not appear spontaneously, but only in the course of a conversation leading over pre-morbid episodes of an emotional determination, for which

reason it may be supposed with some likelihood that his severe *commotio cerebri* has injured the *cortex cerebri* and the association tracts, so that the premorbid episodes of the greatest emotional determination became personal data, which the patient did not realize until his consciousness again began to function, though slowly. His slight euphoria and confabulation during the first part of the second stage of the concussion psychosis then convey the expansive accent to the pictures in his memory that are of emotional determination but still slightly chaotic.

re (D): As has been suggested by several authors, these patients elaborate the accident so that the latter is eliminated, which was also the case with our patient, who had the idea that he was in hospital because of diphtheria, an idea which he stuck to for some months, though gradually with varying tenacity.

As such patients have a complete amnesia as regards the accident, their transformation of the latter to something else must doubtless be considered the outcome of the individual's own need of getting a reasonable explanation of why he is just now in hospital, which he wants to explain to himself during the state of concussion psychosis when his critical sense is practically suspended.

Our patient's idea of having caught a diphtheria may possibly be explained by the fact that—owing to his psychotic manner—the patient was “isolated” during the whole of his stay in the local hospital in a one-bed room in the block generally used for patients with diphtheria, a fact that is known by everybody in the town and its environs. Seeing now that our patient had been admitted to the isolation department and to a one—bed room—and would know nothing of the accident—then it must be quite obvious to the patient that, through his changing faculty of retaining impressions, he would have to draw the conclusion that he had been admitted for diphtheria.

At the after-examination it was impossible to get at the material of which he had formed the idea of having to infect the smaller children of the town with diphtheria. The general vaccination against diphtheria comprising the Danish population

towards the end of World War II is said not to have given rise to the least discussion in the patient's home or among his acquaintances, but he remembered that one day, presumably 15 or 20 years ago, the son of the landlord previously mentioned had told the patient that he would like to be vaccinated against diphtheria; the patient did not remember the reason for this any more.

SUMMARY

A report is given of a case of pseudoparalytic acute concussion psychosis, passing through the three stages described by *Kalberlah*. The expansive-confabulatory syndrome is described and it is attempted to give an explanation of the development of the expansive syndrome (see "re (C)").

In our case the acute picture of the concussion psychosis bears a striking resemblance to the acute paralytic dementia and, consequently, the writers suggest to maintain the term of "pseudoparalytic concussion psychosis," which in this case left the patient with a considerably changed characterological structural formula, so that he must now rather be termed demented to quite a great extent and his appearance now bears a strikingly close resemblance to that of a malarialized paralytic.

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INVESTIGATIONS INTO THE REFLEXES
DURING THE POSTCONVULSIVE STAGE
OF METRAZOL AND ELECTRO-SHOCK
SEIZURES

BY

TORE BROMAN

Disturbances of the reflexes in the postconvulsive stage of spontaneous or therapeutically induced epileptic fits are well-known and have been described by many workers in this field (*Oppenheim* 1913, *Bumke* 1927, *Georgi & Strauss* 1937, *Meier* 1938, *Teglbjærg* 1939, *Strauss, Landis & Hunt* 1939, *Jessner & Ryan* 1942, *de Crinis* 1942, *Kino* 1943, *Kalinowsky & Kennedy* 1943, *Fleischhacker* 1945, *Kalinowsky & Hoch* 1946). After a grand mal fit the following disturbances of the reflexes have been recorded: absence of the light reflex of the pupils (usually the pupils are dilated and exhibit a hippus reaction), absence of the corneal reflex, which is denied by some authors, and of the abdominal and cremasteric reflexes, positive Babinski reflex, sometimes exaggerated muscle reflexes with ankle clonus—sometimes weakened or absent muscle reflexes with atonia (different observations by various investigators).

The examination of the reflexes—especially the pupillary light reflex and the Babinski reflex—is sometimes of practical importance in cases with attacks of unsettled character. The doctor may arrive immediately after the cessation of an obscure seizure and if he is able to establish transitory disturbances of the reflexes there is strong reason to assume that the patient has suffered from a grand mal attack.

For natural reasons it is difficult to collect cases with grand mal seizures of “spontaneous” origin in which it was

possible thoroughly to study the reflexes during the postconvulsive stage. In the present investigations cases of metrazol- and electro-shock seizures have been examined. Even if they may in some respects diverge from ordinary grand mal seizures in epilepsy, important resemblances are obvious and warrant certain conclusions as to common characteristics. In addition to this practical view the purpose of the present investigations was to elucidate the relationship between the different disturbances in the reflexes and suspected variations of the background activity in the central nervous system.

MATERIAL AND RESULTS

The present investigations include two parts, the first of which is a general control of the reflexes registered in the usual way in clinical practice. In the second, electromyographic registration was used for recording the clonic convulsions and the triceps surae reflex (ankle jerk).

Part I. The material comprises 80 cases of psychiatric diseases treated with metrazol- or electro-shocks in the Psychiatric Clinic and in the hospital of St. Lars at Lund in 1946-47. From a neurological point of view they were all normal. The registration of the reflexes was made by myself, not only during the postconvulsive stage, but also before the seizures, besides which the reflexes were controlled in most cases at other times, too.

Most cases (60) were treated with insulin, which was given in combination with metrazol-shock treatment. In four cases grand mal attacks occurring during insulin treatment alone were recorded. In fifteen cases the seizures were elicited by electro-shock. Only three cases of "spontaneous" grand mal attack of epileptic nature were investigated (two of these cases from the Medical Clinic at Lund). In these lastmentioned cases as well as in the four cases with grand mal attacks during insulin treatment, the reflexes of course could not be recorded before the attack, but were completed by a later registration. As the investigations of the metrazol shock cases

were made in a men's department most patients were males.

The reflexes investigated were the pupillary light reflex, the corneal reflex, the abdominal and cremasteric reflexes, the quadriceps reflex (knee-jerk) the triceps surae reflex (ankle-jerk) and the plantar reflex (including the Babinski reflex). In every case the registration was started immediately after the cessation of the clonic convulsions, and the registration was repeated at short intervals until the normal condition was reached. In a few single cases the registration was somewhat incomplete owing to a state of agitation and excitement following the coma. The state of the patients (coma, confusion, reaction to pain and verbal stimuli) during the registration was also noted.

The results of the investigation appear from Tables 1-3. The time values are recorded in minutes from the moment of the last clonic convulsion, which is indicated as 0.

In addition to what appears in the tables the following observations are worth mentioning:

1. The pupils were usually dilated during the period of absent light reflex but they were sometimes of normal size or even contracted (9 cases of 80). Variations of their size was observed almost regularly, mostly rather pronounced (hippus reaction). These observations agree very well with those of earlier investigators.

2. In six cases with metrazol shock there was already before the seizure a clear positive Babinski reflex as an effect of the insulin precoma. Even in these cases this reflex disappeared during a short period (about 2 minutes) after the seizure, but reappeared in all of them.

3. An asymmetry of the reflexes was sometimes observed. Thus, the Babinski reflex could often be recorded during a certain period on one side when it had already disappeared on the other side. The same was the case with the ankle clonus.

4. In the few cases without ankle clonus the triceps surae reflex was nevertheless usually exaggerated during a short period after the seizure. Only in a few single cases was the reflex weak or absent instead, and the control of the reflex be-

TABLE
Postconvulsive stage of

No.	Dose of insulin	Coma	Loss of reaction to		Absence	
			pain stimuli	verbal stimuli	pupill. light	corneal
1	80	—	0—1	0—7	0—1 à 2	0—1
2	40	—	0—2	0—7	0—2	0—1
3	72	(+)	0—1 à 2	0—6 à 7	0—3	0—2
4	152	—	0—2	0—7 à 10	0—4	0—2 à 3
5	80	—	0—2	0—4 à 5	0—4	0—4
6	200	—	0—2 à 3	0—6 à 8	0—2 à 3	0—2
7	104	—	0—2	0—5	0—2	0—1
8	144	—	0—2	0—6 à 8	0—3 à 4	0—2
9	136	(+)	0—3	0—6	0—3 à 6	0—3
10	104	(+)	0—2 à 3	0—5 à 10	0—2	0—1 à 2
11	80	—	0—4	0—5 à 10	0—3 à 4	0—1 à 2
12	120	(+)	0—3	0—10	0—5	0—1 à 2
13	240	—	0—2	0—5 à 9	0—2 à 3	0—2
14	120	—	0—1 à 2	0—8	0—2	0—1 à 2
15	120	—	0—4	0—15	0—6	0—4
16	120	(+)	0—3	0—12	0—3 à 4	0—3
17	136	+	0—5	0—30	0—2	0—4
18	200	(+)	0—2	0—3 à 13	0—2	0—2
19	144	—	0—1 à 2	0—8	0—2	0—1
20	72	(+)	0—2 à 3	0—4	0—3	0—1
21	112	—	0—1 à 2	0—6 à 10	0—2	0—2
22	72	—	0—1	0—12	0—2	0—2
23	104	—	0—1 à 2	0—6	0—2	0—1
24	200	—	0—1 à 2	0—3 à 4	0—1 à 2	0—1 à 2
25	200	—	0—2 à 3	0—4 à 6	0—2	0—2
26	120	—	0—1 à 2	0—2 à 3	0—1 à 2	0—1
27	80	—	0—1 à 3	0—5 à 6	0—1 à 2	0—1
28	72	—	0—1 à 2	0—4	0—2	0—2
29	88	—	0—2 à 3	0—8	0—3	0—1 à 2
30	80	(+)	0—2 à 3	0—7	0—2	0—2
31	72	—	0—1 à 3	0—7	0—3	0—1
32	32	—	0—1 à 2	0—7	0—2	0—1
33	80	—	0—1 à 2	0—5	0—1	0—1
34	96	(+)	0—2	0—6	0—3 à 4	0—1
35	66	—	0—1 à 2	0—10	0—1 à 2	0—1
36	72	—	0—3	0—9	0—1 à 3	0—2
37	80	(+)	0—2 à 3	0—6 à 10	0—2 à 4	0—2 à 4
38	72	—	0—2	0—4	0—2	0—2
39	80	—	0—2	0—7	0—2	0—1
40	120	—	0—1	0—16	0—2	0—2
41	120	(+)	0—2	0—7	0—2 à 3	0—2
42	80	—	0—1 à 2	0—8	0—2	0—2
43	120	—	0—1 à 2	0—6	0—3	0—2 à 3

1
metrazolshock seizures.

of reflexes			Babinski positive	Clonus	
abdominal	cremasteric	plantar		Patellar	Ankle
0—2	0—2	0—12	1—12		0—3
0—3 à 5	0—3	0—3			0—3 à 5
0—7	0—4	0—4	3—4		0—4
0—7 à 15	0—7	0—3 à 6	3—6		
0—4	0—?	0—4	4—4½		
?	0—6?	0—3			0—7
0—4	0—4	0—4 à 6	3—3½	0—2	0—4
0—5 à 8	0—5 à 6	0—9	3—7		0—9
?	0—3	0—3			0—3
0—5 à 10	0—10?	0—5	4—4½		0—5
0—5 à 10	0—5 à 10	0—10	4—5 à 8		0—14
?	0—6	0—5	5?—5½?	0—1	0—10
0—5 à 8	0—5 à 8	0—2			0—2
0—4 à 9	0—4 à 9	0—4 à 9	2—4		0—8
0—15 à 20	0—15 à 20	0—10 à 20	6—10 à 15		0—5
?	?	0—4 à 12	2—4 à 12		0—13
?	?	?	2—20		0—20
0—13	?	0—10 à 13	3—13		
0—18	0—18	0—18	1—18		0—4
?	?	0—2 à 3	2—2½		0—4
0—5 à 10	0—5 à 10	0—14 à 20	3—14	0—1	0—3
0—?	0—?	0—5 à 10	2—5 à 10		
0—2 à 6	0—2 à 3	0—2 à 3	2—2½		0—6
0—2	0—2	0—2	1—1½		0—1
0—4 à 6	0—4 à 6	0—4 à 6	2—4		0—4
0—3 à 5	0—7	0—7	2—7		
0—5 à 10	0—5	0—2	2?—2½?		0—1
0—4 à 8	0—4 à 8	0—2 à 3	2—2½		0—1
0—5 à 10	0—5 à 10	0—5 à 8	4?—4½?		0—2 à 3
0—4	0—4	0—7	5—7		
0—10	0—10	0—6	5—6	0—1	0—1
0—8	0—8	0—2			0—1
0—3	0—3	0—3	2—2½		0—2
0—4	0—4	0—4	2—4		0—4
?	?	0—3 à 4	3—4		0—1
0—10 à 15	0—10 à 15	0—10 à 15	3—10		
?	0—?	0—6			
0—3 à 5	0—3 à 5	0—10	2—8		0—2
0—7 à 10	0—7 à 10	0—7 à 10	2—7	0—1	0—7
?	?	0—16	2—16		0—3
?	?	0—5			0—3
0—10	0—10	0—10	3—10		0—4
0—3	0—3	0—3			0—1

TABLE

No.	Dose of insulin	Coma	Loss of reaction to			Absence
			pain stimuli	verbal stimuli	pupill. light	corneal
44	96	(+)	0—2	0—7	0—3	0—2
45a	96	—	0—2	0—4	0—2	0—2
45b	120	—	0—2	0—7	0—3	0—2
46	88	—	0—2	0—15	0—2	0—2
47	32	—	0—2	0—8	0—2	0—2
48	64	—	0—2	0—6	0—2	0—1
49	112	—	0—2	0—7	0—2	0—2
50	88	—	0—2	0—5	0—2	0—2
51	80	—	0—3	0—5	0—3	0—2 à 3
52	120	—	0—2	0—6 à 9	0—2	0—1
53	104	(+)	0—5	0—10	0—2	0—2
54	88	(+)	0—2	0—10	0—2	0—1
55	56	—	0—3	0—7	0—3	0—1
56	64	—	0—2	0—5	0—1 à 2	0—1
57	120	—	0—3	0—7	0—3	0—1
58	80	—	0—2	0—6	0—2	0—1
59	96	—	0—2 à 3	0—9	0—2 à 3	0—1 à 2
60	140	—	0—2	0—7	0—3	0—1

fore the seizure proved that this was usually the case in these patients also during normal circumstances. Similar observations were made on the quadriceps reflex (knee jerk), but this reflex was more often weaker after the seizure.

A combination of the results from Tables 1-3 is seen in Table 4, which shows the average duration of the postparoxysmal reactions and their approximate frequency. The duration of the different reactions is assigned in minutes recorded from the cessation of the convulsions.

It is apparent that there is no tangible difference in the postparoxysmal reaction of the different kinds of seizure. A prolonged duration of the disturbances in the reactions could be expected in the metrazol-shock cases owing to the simultaneous effect of the insulin. This action, however, is rapidly abolished by an administration of saccharose through a gastric tube, and in most cases the insulin dose given in the days of metrazol treatment was too small to cause any marked effect

1 (cont.)

of reflexes			Babinski positive	Clonus	
abdominal	cremasteric	plantar		Patellar	Ankle
?	0—4	0—4	—	—	0—1
0—3 à 4	0—3 à 4	0—4	3—3½	—	0—1
0—4	0—4	0—6	5—5½	—	0—1
?	0—10 à 15	0—10	5—7	—	0—2
0—4	0—2	0—4	3—3½	—	—
0—5	0—2	0—7 à 10	3—7 à 10	—	—
0—5 à 8	0—5 à 8	0—5 à 8	—	—	0—5
0—3	0—3	0—3	—	0—2	—
0—5 à 10	0—5 à 10	0—10	3—10	—	0—3
0—5	0—5	0—10 à 20	4—10	—	0—2
0—6 à 8	0—6 à 8	0—6 à 10	3—3½	—	0—10
0—5 à 10	0—5	0—10	3—10	—	0—5
?	0—4	0—6	3—6	—	0—5
0—7 à 10	?	0—5	2—2½	—	0—2
0—10	0—8	0—20	3—13	—	0—3
0—5	0—5	0—5 à 9	5—5½	—	—
0—5	0—4	0—3	—	—	0—1
0—6 à 9	0—6	0—9 à 15	4—9	—	0—5

on the reflexes. The gastric tube inserted through the nose in these cases acted as a strong pain stimulus and may have been partly responsible for the shortness of the postparoxysmal coma and early reaction to pain recorded.

It may be of practical interest to note that the positive Babinski reflex could usually be recorded only during a rather short period—in almost half of the cases only ½-2 minutes.

Part II. The investigations were completed by an electromyographic registration of the electrical activity in the triceps surae and tibialis ant. muscles during and immediately after the convulsions. The purpose was to find out whether the exaggeration of the muscle reflexes (ankle clonus) was demonstrable immediately after the convulsions and if it was correlated to a possible lasting activity of central origin in the muscles. The existence of such an activity is supported by the impression that the muscles sometimes exhibit a certain tension also after the cessation of the convulsions.

TABLE 2
Postconvulsive stage of electro-shock seizures.

No	Sex	Loss of reaction to		pupill light	Absence of reflexes					Babinski positive	pat.	Clonus	
		pain stimuli	verbal stimuli		corneal	abdomi- nal	cremasteric	plantar	ankle				
1	♀	0-2	0-7	0-2	0-1	0-5		0-12 à 20	2-12	0-1	0-2		
2	♀	0-1 à 2	0-5 à 8	0-2	0-1	0-20		0-8 à 13	2-8	—	0-1		
3	♀	0-2	0-6	0-2 à 3	0-2	0-5		0-4	3-3½	—	0-2		
4	♀	0-2 à 3	0-4 à 5	0-2	0-2	0-2 à 3		0-3	2-2½	—	—		
5	♀	0-3	0-4 à 5	0-1	0-1	?		0-3	—	—	0-1		
6	♀	0-2 à 3	0-6	0-2	0-1 à 2	?		0-3	—	0-2	0-2		
7	♀	0-4	0-8	0-2	0-1	0-6		0-2	—	—	—		
8a	♀	0-3	0-6 à 7	0-2	0-1 à 2	0-5		0-2	—	—	—		
8b	♀	0-3	0-7	0-2	0-1 à 2	0-7		0-2	—	—	—		
9a	♀	0-2	0-6	0-1	0-1	0-6		0-20	3-20	—	0-8		
9b	♀	0-2	0-6	0-1	0-1	0-5		0-25	3-25	—	0-4		
10a	♀	0-3 à 4	0-8 à 10	0-1 à 2	0-1 à 2	0-8 à 10		0-20	—	—	0-3		
10b	♀	0-2	0-10	0-2	0-2	0-10		0-6	2½-2½?	—	0-2		
11	♀	0-3 à 4	0-6	0-2 à 3	0-1	0-5	0-5	0-4	—	—	—		
12	♀	0-2	0-3 à 4	0-2 à 3	0-2	0-6	0-4	0-3	—	—	0-1		
13	♀	0-2 à 3	0-6	0-2	0-1 à 2	0-8	0-6	0-6	2-5	—	0-2		
14	♀	0-2	0-5	0-2	0-1	0-5	0-5	0-4	—	—	0-1		
15	♀	0-3	0-7	0-2	0-1	0-10	0-8 à 10	0-10	2-9	0-1	0-2		

TABLE 3
Postconvulsive stage of "spontaneous" epileptic fits (in cases with and without insulin treatment).

No.	Dose of insulin	Loss of reaction to			pupill.	Absence of reflexes			Babinski positive	Clonus	
		pain stimuli	verbal stimuli			corneal	abdominal	cremasteric		patellar	ankle
1	80	0-2	0-10		0-3	0-2	?	?	—	—	0-2
2	200	0-2	0-8 à 10		0-2	0-1	0-13	?	2-9	0-2	0-4
3	140	0-3 à 4	0-7		0-2	0-1	0-7	0-7	—	—	0-2
4	180	0-2	0-4		0-2	0-1 à 2	0-5	0-5	2-3	—	—
5	—	0-3 à 4	0-8		0-2	0-2	0-6	0-6	3-7	—	0-6
6	—	0-3	0-7		0-3	0-1	0-8	0-6	3-5	—	0-5
7	—	0-2	0-5		0-2	0-1	0-5	0-4	2-4	0-1	0-3

TABLE 4
*Approximate frequency and average duration of different reactions
 in the postconvulsive stage.*

Reactions	Percentage frequency in the whole mtrl.	Duration in		Spont. fits
		Metrazol-shock	Electro-shock	
Loss of reaction to pain stim.	100	0—2 à 3	0—2 à 3	0—2 à 3
Loss of reaction to ver- bal stimuli	100	0—5 à 10	0—5 à 8	0—5 à 8
Abs. of pupill. refl.	100	0—2 à 3	0—2	0—2
„ „corneal +”	100	0—1 à 2	0—1 à 2	0—1 à 2
„ „abdom. +”	100	0—5 à 10	0—5 à 10	0—5 à 10
„ „cremast. +”	100	0—5 à 10	0—5 à 8	0—4 à 7
„ „plantar +”	100	0—5 à 15	0—2 à 20	0—4 à 10
Babinski pos.	75	2—(10 à 15)	2—(10)	2—(9)
Patell. clonus	14	0—1 à 2	0—1 à 2	0—1 à 2
Ankle „	75	0—4 à 10	0—1 à 4	0—2 à 6

The electromyographic records were taken in 12 cases of electro-shock and in 12 cases of metrazol-shock. Subcutaneous electrodes were used, in most cases with one pair of electrodes in the triceps surae sin., one pair in the tibialis ant. sin., and one pair in the triceps surae dx. Fig. 1 shows the general sequence of events during a metrazol-shock. At first some irregular clonic contractions are seen—synchronous in all leads¹. This phenomenon is not met with in electro-shock cases or in spontaneous fits—a well-known fact in the literature. A state of tonic cramp soon follows. This state gradually develops into high-frequent clonic convulsions, the frequency of which gradually decreases until ultimately the fit is over and complete inactivity is seen. The intervals between the last clonic twitchings are usually 50—150 cs, and towards the end the spike groups have a duration of 20-30 cs.

Sometimes there occurs a certain asymmetry in the clonic

¹ and not alternating between agonists and antagonists as in the arm muscles according to *Strauss & Landis* (1938).

twitchings, either in the form of some asynchronous contractions in both legs (cf Fig. 3a) or by an earlier cessation of the convulsions in one of the legs (cf Figs. 2a and 3a). The gradual decrease in frequency of the clonic twitchings apparently depends not only on an increase of the time intervals, but also on a gradual weakening and disappearance of some convulsions (Fig. 3a and b), indicating that different (right- and leftsided?) centres may be responsible for the different (alternating?) twitchings.

The ankle jerk was elicited by taps with a reflex hammer on the anterior part of the sole, with the foot held in a position of dorsal flexion. The repeated taps were made with about the same strength and a possible clonus could be studied by the fixed position of the foot. The most common result is demonstrated by Fig. 2. At first a single reflex spike is seen immediately after the last clonic convulsion. This initial spike is, however, soon followed by an increasing number of spike groups, indicating a tendency to clonus which usually becomes manifest within 2 seconds.

Repeated registrations at short intervals after the end of the fit showed that the state of inactivity after the last clonic jerk of the seizure usually persisted for about 2 minutes, i.e. about the same time after which the clonus disappeared and the Babinski reflex became apparent. After about 2 minutes, however, a "spontaneous" activity was usually apparent not only electromyographically but also in the behaviour of the patient, spontaneous movements were seen and reaction to pain stimuli were demonstrable. In a few cases, however, the "spontaneous" activity of a tonic character appeared earlier—in a case of electro-shock already after 4-5 seconds (Fig. 2b). And in three cases, treated with insulin and metrazol, a pronounced activity of a tonic character was seen all the time, during the intervals between the clonic twitchings as well as immediately after the cessation of the convulsions (Fig. 2c). In spite of this, their reactions to pain stimuli and their reflex reactions followed the common pattern outlined above, but with the exception that clonus was elicitable immediately after

the last clonic convulsion. This aberration was, however, demonstrable also in some cases without any form of spontaneous activity (Figs. 3a and b) and, furthermore, it could even be demonstrable during the intervals between the clonic convulsions. Thus, the results differed rather much in character.

DISCUSSION

In previous literature there are some discrepancies in the descriptions of the postconvulsive reactions after grand mal seizures.

The muscle reflexes are sometimes supposed to be weakened immediately after a fit with a later demonstrable exaggeration (*Teglbjærg* 1939, *de Crinis* 1942, and others). *Jessner* and *Ryan* (1942) found clonus of the foot in cases of metrazol-shock seizures, but absence of the deep reflexes (as well as the superficial ones) immediately after an electro-shock seizure, later, however, (after a minute or two) the tendon jerks were brisk and exaggerated. Contrary to these statements *Meier* (1938) in a study on metrazol-shock seizures claims that all the muscles of the body at first remain in a state of tonic tension and that the exaggeration of the muscle reflexes shortly afterwards passes into a state of weakened reflexes. According to *Kino* (1943), who made a comprehensive study of the reflexes in the postconvulsive phase of electro-shock seizures, the following statements could be made: "As a rule the *deep reflexes* are greatly exaggerated during the first minutes . . ." "Clonus can be easily set up at the ankle and in favourable cases at the knee—and wrist. An ankle clonus is constant during the first minute, patellar-clonus is a rare occurrence."

"Gradually all deep reflexes lose their briskness and return after approximately five minutes to their original condition. This is the rule. In a small number of cases, however, some of the deep reflexes may be decreased or even completely abol-

ished in the first one to three minutes or after a short preliminary exaggeration only."

"Not all of the deep reflexes are apt to be abolished in the same way. The knee-jerk is the most prone to disappear, less frequently the ankle jerk, then the biceps and finally the pronator jerk."

These findings are confirmed by other authors, such as *Kalinowsky & Kennedy* (1943) and *Kalinowsky & Hoch* (1946), and they are also in agreement with the present investigations. It may be added here that the presence of muscle reflexes can be demonstrated already *during* the clonic stage of the seizures and that they are sometimes exaggerated (clonic) already at this stage, even if the commonest occurrence is a gradual increase to clonus of the triceps surae reflex during a few seconds after the last convulsion.

Spontaneous activity during the postconvulsive stage is discussed by several authors. Thus, in metrazol-shock cases *Kino* (1943) found: "In the first minutes after the cessation of convulsive jerks the limbs are still in marked hypertonus, the arms very often perform a slow bending movement and in many persons a vivid play of myoclonic contractions can be observed. The duration of this state varies widely from individual to individual, the average duration is approximately five minutes." The same phenomenon was observed by *Kalinowsky & Kennedy* (1943): "Closer observation revealed that metrazol patients have sporadic twitchings in increasing intervals after the clonic phase is over." And they explained this activity as "due to the effect of the circulating drug which, after the convulsion, is again able to stimulate cortical cells. Postconvulsive twitchings do not occur in electric convulsions."

These statements are supported by the present investigations. In three cases a continuous activity was recorded during and after the convulsive stage—and all these cases belonged to the metrazol group. Probably more of these metrazol cases would have exhibited such activity if the registration in the present investigations had also included the arm muscles.

The explanation given by *Kalinowsky & Kennedy* that this activity is due to the prolonged action of the drug on the central nervous system sounds reasonable, but it must be pointed out that this effect is demonstrable not only *after* the seizure but also *during* the intervals of the clonic convulsions, as was shown in the present investigations. Thus it must be due to a stimulation of centres other than those that give rise to the convulsions, and the activity may probably arise from other cells than those in the cortex. Investigations about the possible correlation between brain potentials and muscular activity during epileptic seizures (in cases with "spontaneous" fits) also suggest that the manifestation of the muscles in many instances are of subcortical origin (*Jasper & Andrews*, 1938).

The most common appearance of spontaneous activity after a seizure was, however, seen after a lapse of about two minutes. At this stage it had the character of a returning normal motility. Thus it corresponded with a returning of other, primitive functions such as a general reaction to pain stimuli, and a positive Babinski reflex; and the first spontaneous movements were seen at about this time, even if the subject was still in a state of profound mental confusion.

It thus seems as if there are two different kinds of spontaneous activity after a seizure. One early form is seen in some of the metrazol cases, probably due to the action of the drug, and another late form is seen in all cases when their reactions to environmental stimuli are returning. That these two kinds of activity really are different is supported by the fact that the early form of activity is accompanied by exaggerated muscle reflexes and by the absence of even pathological skin reflexes, while the late form appears at a time when the Babinski reflex becomes manifest and the muscle reflexes begin to decrease to their normal degree.

We now arrive to the special and more far-reaching problem, viz. *the causes of the exaggeration of the muscle reflexes*. Two different theories are discussed in the (neurological) literature; according to the old theory an exaggeration of muscle

reflexes is seen as the result of the liberation of the spinal reflex centres from inhibitory impulses coming along the suprasegmental tracts. This was the common explanation for the origin of exaggerated muscle reflexes in cases with lesions of the pyramidal tracts. Later, *Hoffmann* (1922, 1934) points out a series of arguments against this theory and in favour of a totally different explanation, i.e. the idea that subliminal impulses from suprasegmental tracts constitute a condition necessary for a stimulation of the motoneurons by afferent impulses from the muscle spindles. If these suprasegmental impulses are few, the reflexes will be weak. If they are numerous but still subliminal, the reflexes will be exaggerated. If some of the suprasegmental impulses are liminal, a "spontaneous" activity will of course be seen, but the reflexes may still be exaggerated if most impulses are subliminal. If the number of liminal impulses increases, the reflex will be weaker and ultimately disappear as a consequence of a disengagement of the muscle receptors by the contracting fibers (*Fulton & Pi-Suñer*, 1928).

The whole problem is rather complicated, as stimulating impulses coming from higher centres may have different effects, both quantitatively and qualitatively, on the muscle reflexes if they come from different centres and pass through different tracts with different frequencies.

The results of the present limited study of the reflexes in the postparoxysmal state disagree with neither of the above mentioned theories, yet it seems to me as if the results harmonize best with *Hoffmann's* theory. Thus the following facts are obvious:

(1) Manifest ankle clonus is seen during a state with a continuous activity of central "origin" (in cases with the early form of spontaneous activity).

(2) In most cases when an ankle clonus is elicitable in the postparoxysmal state a few seconds after the last convulsion, a probable explanation is the existence of a central activity (a kind of after-activity?) with subliminal impulses of a gradually increasing character (the weakness in the beginning

due to exhaustion?). If we assume that these central impulses remain as subliminal, their only effect will be a rapid increase in the exaggeration of the muscle reflexes - as was demonstrated in the present investigations. If in isolated cases the central impulses increased to become liminal, an increasing "spontaneous" activity would be seen in the muscles shortly after the fit - a phenomenon also met with in a few cases in the present investigations. In some investigations of muscle action potentials in the period of prodromal muscular jerks in myoclonic epilepsy *Dawson* (1946) also comes to the conclusion that a clonic exaggeration of the knee jerk is the result of an increased number of subliminal impulses from cerebral centres.

Various authors report the appearance of a *Babinski reflex* in a varying and rather low frequency during the postparoxysmal stage (in less than one third of all cases according to *Kalinowsky & Kennedy*). These variations presumably to a great extent depend on the question whether the reflex was tested often or not. In the present investigations a positive Babinski reflex was manifest in the majority of cases (75 per cent.), but it was often a rather transitory phenomenon, demonstrable only during a short period— $\frac{1}{2}$ -2 minutes in about half of the cases. Another fact of importance is that the *Babinski* reflex hardly ever appeared during the first 2 minutes after the convulsions. When trying to demonstrate a positive *Babinski* reflex it is thus of importance not to restrict the examination to a single test, but to repeat the examination several times during some minutes after the first period of exteroceptive areflexia (from 2 to 5 minutes after the seizure).

The absence of even pathological skin reflexes during the first minutes of the postconvulsive stage was shown by *Kino* (1943) and forms a contrast to the exaggeration of the muscle reflexes at this stage. In most neurological manuals these two phenomena are supposed to be correlated. The dissociation during the postconvulsive stage between the spastically exaggerated muscle reflexes and the appearance of a positive *Babinski* reflex is, however, in agreement with the statements

by *Fulton & Kennard* (1934), according to which they can be caused separately by lesions of different cortical regions in primates.

The corneal reflex is pointed out by *Kino* (1943) to be "the only superficial reflex which is not inhibited by the convulsive discharge." "... immediately after cessation of the jerks the reflex is invariably present. The first reactions are not so brisk as the normal response though their amplitude is quite normal." This statement is referred to by *Kalinowsky & Hoch* (1946), but in the present investigations I have come to the opposite conclusion. The corneal reflex was found to be invariably absent during a very short period after the last convulsion (about 1 minut).

In trying to make a *survey of the results* of the present investigations of the reflexes during the postconvulsive stage, I find that they may be suitably classified into three phases. During *the first phase* there is an exteroceptive areflexia usually combined with an exaggeration of the muscle reflexes (i.e. the most simple form of reflexes) and a reappearance of the automatical functions—breathing. Both of these functions may appear already during the clonic stage of the seizure.

Then follows *the second phase* with returning exteroceptive reflexes, especially reflexes elicited by nociceptive stimuli, and a waning of the exaggeration of the muscle reflexes. At first the corneal reflex appears, then the pupillary light reflex and later the Babinski reflex, which is at first the only apparent skin reflex. During this stage the subject also starts to react to pain stimuli by withdrawal reactions of the arms, and spontaneous movements are seen, but he is still mentally confused.

The third phase is characterized by a gradual reappearance of the normal skin reflexes (the abdominal reflexes are the last to return) and the subject starts to react to verbal stimuli, but is still more or less in a state of confusion.

It is not, of course, possible to draw sharp border-lines between these three phases, they overlap one another. For example the first phase may be said to last about 2 minutes,

with the second phase starting already after about 1 minute with the reappearance of the corneal and then the pupillary light reflexes. The second phase can be said to pass into the third phase about 5 minutes after the cessation of the convulsions, whilst this last phase has a duration of about 5 minutes.

Some results of practical significance are worth mentioning. In a clinical investigation of a patient who has just suffered from an obscure kind of convulsions the examination of the reflexes should be made with regard to the time which has elapsed after the cessation of the attack. Immediately afterwards it is specially important to examine the pupillary light reflex, the corneal and plantar reflexes, and the ankle jerk. When examining the pupillary light reflex it is of importance to consider the possible presence of a hippus reaction. A contraction of the pupils when exposed to light should always be checked in order to exclude the possibility of the contraction being due to a hippus reaction occurring independently of the light. The examination of the plantar reflexes should not be restricted to a control of a possible Babinski reflex. The mere absence of the normal plantar reflexes is of equal importance, provided that it can be shown that the normal reflexes appear within a few minutes. This is demonstrable in all cases of grand mal seizures, but the Babinski reflex does not appear in about 25 per cent. When trying to demonstrate a Babinski reflex it is of importance not to restrict the examination to a single attempt if it is negative, but to repeat the examination several times during the first 5 minutes.

If several minutes have elapsed after the cessation of the convulsions there is little chance of demonstrating any abnormalities in the pupillary light reflexes or the corneal reflexes, and the ankle clonus might have disappeared. It is then better to concentrate the examination on the skin reflexes. A Babinski reflex might persist during more than 10 minutes after a grand mal attack, but at this stage one more often finds an absence of the abdominal and cremasteric reflexes (usually 5-10 minutes after a grand mal seizure) as the only pathological

reflex phenomenon. If their absence has been demonstrated the examination must of course be completed by a later control of the patient to be sure that they are present during ordinary conditions.

It may be added that the above-mentioned views apply only to cases with grand mal seizures. Epileptical fits of so many kinds occur that the demonstration of normal reflexes after an attack of an obscure kind does not exclude the possibility that it has been of an epileptic nature. Only a positive finding is conclusive. On the other hand, it does not point to the cause of the disease. A demonstration of asymmetrical reflexes, thus, does not prove the existence of a local cerebral lesion—the appearance of a unilateral Babinski reflex or unilateral ankle clonus during part of the postconvulsive stage is not an uncommon finding after ordinary grand mal seizures—a fact pointed out by several investigators.

SUMMARY

The purpose of the present investigations was to study the reflexes during the postparoxysmal state in metrazol- and electro-shock seizures. The material was supplemented by a few cases of “spontaneous” epileptic fits. In some of the cases an electromyographic registration of the events during the seizure and the postparoxysmal state was made.

Generally three phases of the postparoxysmal state could be discerned. During the first phase there was a total exteroceptive areflexia with a persistence of the most simple reactions only, the breathing movements and the two-neuron-reflexes. The last-mentioned reflexes (the muscle reflexes) were—as stated by *Kino* and *Kalinowsky et al.*—exaggerated in most cases during the first phase. In most cases, however, this exaggeration did not appear immediately after the cessation of the convulsions, but after a lapse of about 2 seconds. It is discussed whether this exaggeration was due to a subliminal after-activity in the spinal tracts. In a few cases of metrazol-shock seizures there appeared a continuous activity

during the intervals between the convulsions as well as immediately after the cessation of the convulsions. This phenomenon pointed to a persistent action of the drug and to differences in the effect on different regions of the central nervous system. This early form of continuous activity was associated with exaggerated muscle reflexes as opposed to the later spontaneous activity during the second phase of the postparoxysmal stage. In this phase the subject starts to react to nociceptive stimuli and the first exteroceptive reflexes are seen (first the corneal reflex, then the pupillary light reflex and later the Babinski reflex), while the exaggeration of the muscle reflexes wanes until the reflexes are of normal briskness. Thus, the positive Babinski reflex (demonstrable in about 75 per cent. of the cases) and the exaggeration of the muscle reflexes are dissociated phenomena. During the third phase—from about 5 to about 10 minutes after the cessation of the convulsion—the normal skin reflexes reappear, and the subject—still in a state of confusion—begins to react to verbal stimuli.

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THE HISTOPATHOLOGICAL REACTION OF THE AREA POSTREMA

BY

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A small structure known as the area postrema which is situated in the dorsolateral part of the medulla on each side and presents in the caudal portion of the fourth ventricle has been the subject of several anatomical studies (*Retzius* 7, *Blake* 2, *Streeter* 9, *Wilson* 10, *Wislocki* and *Putnam* 13 a & b, *Wislocki* and *King* 12, *King* 6, *Wislocki* 11, *Cammermeyer* 4 a & b). It is composed of a rich plexus of sinusoids which enmesh numerous melanin pigmented nerve cells, has an extremely loose neuropile, and is covered with a single layer of flattened ependymal cells all of which serve to delimit it from the surrounding tissue. In marked contrast to the vessels of the brain, the endothelium of the sinusoids is permeable to acid semicolloid dyes (*Wislocki* and *Putnam* 13 a & b, *Wislocki* and *King* 12, *King* 6, *Skoog* 8 a & b, *Broman* 3). There can be little doubt therefore that the area postrema differs both anatomically and histofunctionally from ordinary brain tissue. Some few observations, already published by one of us (*J. C.* 4 a & c) would indicate that a similar distinction holds

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true in certain pathological conditions. In three cases of hemochromatosis iron was deposited in glial cells and the lining ependymal cells of the area postrema, whereas no iron could be demonstrated in general paresis, pernicious anemia, diabetes mellitus, eclampsia, liver cirrhosis, acute agonal hemorrhages and subarachnoid hemorrhage from a ruptured sacular aneurysm of the vertebral artery. That the area postrema has, however, a close relationship to nervous tissue is established by the presence of Nissl granules in the nerve cells and by the increasing amounts of cytoplasmic lipochrome and melanin with advancing age. Also, like certain other nerve cells, those in the area postrema were filled with lipoid and appeared pale, swollen and vacuolated in one case of amaurotic family idiocy.

In reviewing the material collected for some years at the Neuropathology Laboratory of the Boston City Hospital it was possible to compare the pathological reactions of the area postrema to other parts of the nervous system in a large variety of diseases. Since the original sections were usually single and were taken at random from the caudal part of the medulla the scope of our study is restricted to the qualitative aspects of the tissue reaction. An additional handicap was the variability of the staining methods which had been used in the different cases.

The type of available material has naturally shaped the aim of the present communication, which has been first to study more generally the mode of action of the cellular elements of the area postrema, and secondly, to determine the changes which occur with aging process, intracranial hemorrhages, inflammatory and other miscellaneous diseases. This material was not suitable for evaluating the effects on this area of metabolic diseases or disturbances of the cerebrospinal fluid circulation and the systemic blood pressure.

THE EFFECTS OF AGE

From birth to old age a continuous series of changes take

place. In the newborn the nerve cells are closely packed together in rounded or elongated gland-like clusters which are separated by strands of a loose neuropile, sinusoids and thick-walled arteries, Pl. I, Fig. 1 & 2. The sinusoidal loops often radiate from the base towards the ventricular surface in a fan-shaped arrangement. In adult life only a few of the nerve cells retain these acinar formations, the others becoming diffusely scattered through the area postrema. An increasing number of these cells come to occupy a position just beneath or between the ependymal cells. We were unable to determine whether this apparent displacement of nerve cells is due to a migration from the ventrolateral to a dorsomedial position or to a stretching of the area postrema as the fourth ventricle enlarges.

In infancy and childhood the nerve cells are generally small and extremely pale because of poor development of Nissl granules. Not infrequently, however, even in the newborn a few Nissl granules can be recognized, as in one of our cases of erythroblastosis fetalis dying on the 4th or 5th day of life. Nissl granules were much more conspicuous in the 7th month of life. In adults the number and size of Nissl granules is quite variable. Indentation of nuclei, clear spaces, cytoplasmic "vacuoles" next to nuclei, binucleated or multinucleated nerve cells and arrangement of cells in pairs were observed in some cases, P. II, Figs. 3, 4 & 5. These changes were observed more in the older age groups, but their significance is unknown. Fibrillary changes and senile plaques were not found in the area postrema of old persons, up to 80 years, nor in Alzheimer's disease.

Neutral fat is not present in infancy and childhood. In a male 5 years of age, dying of cerebral contusion and laceration, and in a female 6 years of age, succumbing to post-measles encephalomyelitis the nerve cells of the areae postremae were free of fat (lipochrome). At the age of 13 minute amounts of fat appeared in thionine stained sections as faded yellowish granules, and by the age of 15 these granules appeared to be discrete and clearly sudanophilic. In cases of amyotrophic

lateral sclerosis there were abundance of small particles which stained a pale orange in Sudan O-R-O, and a light yellow in thionine. The amount of fat was invariably increased in late life and though less abundant, corresponded roughly to that found in other nerve cells.

Minute particles of dark green to black material gradually increased in amount with age. These granules, adjudged to be melanin, had an affinity for silver and could be demonstrated by a variety of methods. In this respect the staining properties of these cells resembled those of the substantia nigra and the pigmented nuclei of the brain stem. In three newborn with erythroblastosis fetalis and kernicterus and in two cases dying at 4½ months of age, from hemorrhage in the adrenal cortex and post-measles encephalomyelitis, respectively, no silver impregnated granules were seen. In a 25 year old case of multiple sclerosis there was a moderate amount of melanin in the nerve cells. After the third decade the melanin increased greatly; some of the cells were completely filled with this pigment. However, even in late life some of the nerve cells in the depth of the area postrema were either sparsely or not at all pigmented.

One or two mast cells were frequently seen in the area postrema. The number of these cells seemed to increase in various conditions especially hemorrhagic and infectious diseases. This appearance of mast cells as a reaction to noxious agents was observed as early as 3¼ years of age in a patient succumbing to acute bacterial leptomeningitis with the Waterhouse-Friderichsen syndrome. Here 13 mast cells were observed in one paraffin section 6 microns in thickness. In another case dying from cerebral edema after a head injury there were 11 mast cells in 2 microscopic sections. As many as 32 mast cells were found in 3 sections from a 5 year old boy who died of toxic encephalopathy after chickenpox. In infants and young children no definite reaction of the mast cells was demonstrable, but this negative finding has little value since the area postrema was not cut in serial sections and death may have intervened before the reaction of these could take place. One

was a case of erythroblastosis fetalis¹ with subdural and subarachnoid hemorrhages dying on the 6th day after birth and the other was a case of intraventricular hemorrhage of one day's duration, which caused death at 11 months of age. Unlike the white matter of the neonate brain, a diffuse metachromasia of the tissue of the area postrema was not observed.

Finally some reference should be made to glial cells. Microglial cells with irregular, elongated nuclei are found beneath the ependymal lining, as well as in the medulla adjacent to the ventrolateral border of the area postrema of newborn (in a case of erythroblastosis fetalis dying at 6 days of age; in a case of a premature infant with congenital icterus and malnutrition dying at 2 weeks of age; in a premature infant with atelectasis at 13 hours of age). Microglial cells of similar appearance were observed at a somewhat later age under the ependyma of the neighbouring ventricular wall, and in the funiculus separans. It was extremely difficult to make a detailed study of the astrocytes and the oligodendrocytes because they were rarely present in any sizable number. Any alteration of these cells when present was probably related to the disease in question more than to ageing.

HEMORRHAGES

In our cases we were unable to discern any correlation between hemorrhages in the area postrema and the clinical events of the illness. Hence these changes are of greater morphological interest than clinical significance. The material can be subdivided into three groups, i.e. A. hemorrhages into the cerebrospinal fluid spaces, B. hemorrhages of traumatic origin within the area postrema, and C. agonal hemorrhages in the area postrema.

A. Hemorrhages into the Cerebrospinal Fluid Spaces.

In the acute stages (1-4 days) of subarachnoid hemorrhage

¹ Changes attributable to this disease were absent in the area postrema.

from ruptured saccular aneurysms or from traumatic brain laceration no free iron (Turnbull blue method) could be demonstrated in the area postrema. In cases where the subarachnoid hemorrhage had been present for about 6 days there were hemosiderin in macrophages of the leptomeninges, in the choroid plexuses and sometimes also in the area postrema. Usually only a few small hemosiderin granules in macrophages appeared around the vessels in the depths of the area postrema or the vessels delimiting the taeniae and the areae postremae laterally. In one instance, however, the amount of hemosiderin was greater, being present in scattered glial cells all through the area. One gained the impression that the iron containing material had diffused from the subarachnoid spaces along the vessels which enter the areae postremae from the dorsolateral direction.

It has already been pointed out that the area postrema not infrequently contains mast cells. In cases in which subarachnoid hemorrhage had occurred four weeks before death the number of mast cells had increased moderately. In other cases of subarachnoid hemorrhage mast cells were present in the usual small number or were absent. Therefore our material does not permit any conclusions to be drawn as to the significance of this reaction.

B. Traumatic Hemorrhages in the Area Postrema.

A rather unusual opportunity to study the effects of local trauma was afforded by a case in which death occurred 2 days after a suboccipital cisternal puncture. The patient was an elderly woman with cerebral arteriosclerosis who had been admitted to the hospital because of a sudden onset of flaccid paraplegia after a fall. Because no cerebrospinal fluid could be obtained by lumbar puncture a cisternal puncture was performed, allegedly without complications. After this procedure the condition of the patient improved for around 48 hours. She then lapsed into coma and died about an hour later. At autopsy there was a clot of blood attached to the choroid

plexus of the fourth ventricle in the calamus scriptorius, which was excavated as demonstrable in Pl. II, Fig. 6. Rostral to this there were two minute hemorrhages, pinpoint in size, in the midline at the level of the abducens nuclei. When the clot was removed the areae postremae were hemorrhagic. These hemorrhages, as viewed in cross sections, were along the lateral border of each area postrema and in the lower medulla fused into a larger triangular mass situated in the midline posterior to the central canal. In microscopic sections there were minute foci of complete necrosis of the tissue around the hemorrhages at the level of the abducens nuclei in the midline. At the border of the necrotic tissue numerous pleomorphic microglial cells and some neutrophilic leucocytes were present, and the endothelial and adventitial cells of small blood vessels had proliferated. The overlying ependyma was partly disrupted and necrotic. On serial sections the larger hemorrhages appeared laterally to the area postrema on each side and separating it and the taenia from the remainder of the medulla, situated in undamaged tissues. A thin layer of flattened ependymal cells delimited the hemorrhages along their ventricular aspects dorsally. The hemorrhages extended ventrolaterally and caudally from the area postrema as far as the dorsal and vagal nuclei. The nuclei of the dorsal funiculi were damaged and displaced ventrolaterally. There was hemorrhage in the subarachnoid space next to the choroid plexus of the lateral recesses and the subarachnoid veins over the same parts of the medulla were filled with fibrin and neutrophile, *i.e.* acute thrombosis.

On the basis of these anatomical findings it was decided that the hemorrhage of the areae postremae and taeniae was secondarily caused by accidental trauma during cisternal puncture. The intensity of the neutrophile leucocyte infiltration, the glial and vascular reaction together with a rather discrete hemosiderin formation in the minute necroses would correspond to the lapse of time between trauma and death. As a terminal event probably occurring shortly before death larger hemorrhages had dissected the areae postremae bilater-

ally. This latter event might have been due to thrombosis of the aforementioned subarachnoid vessels.

Another case also relevant to this matter of traumatic hemorrhage was that of a boy who fell down an elevator shaft and died a few hours later. At autopsy the cerebrum and cerebellum were severely contused, lacerated and edematous. The areae postremae were the site of numerous small fresh hemorrhages, which were visible in the gross material.

C. Agonal Hemorrhages.

Small hemorrhages confined to the Virchow-Robin space are often found post-mortem subependymally in the floor of the fourth ventricle, the wall of the third ventricle and aqueduct of Sylvius. Depending on their size they may be seen grossly or discovered only during microscopic examination. *Duret* (5), who originally observed these hemorrhages in cranial injuries, commented on their frequent location at the caudal end of the fourth ventricle. Later, however, *Berner* (1) noted similar hemorrhages rostral to the medullary striae of the fourth ventricle. Various hypotheses as to the cause and significance of these hemorrhages have been offered, but most pathologists have come to the conclusion that they are "agonal".

In our material of sections from the caudal end of the fourth ventricle well-delimited perivenous hemorrhages of "agonal" nature were found in 3 cases. In one case, a 17 year old male, the hemorrhage had invaded the dorsal motor nucleus of the vagus nerve. Another case, a 76 year old female, who had died from thrombopenic purpura, exhibited hemorrhages of "agonal" type in the area postrema. In addition a small meningioma, attached to the superior sagittal sinus, was surrounded by quite massive hemorrhage and necrosis of brain. A temporal lobe pressure cone and many small hemorrhages in the midbrain and pons were also present. The hemorrhages in the areae postremae penetrated diffusely into the perivascular tissue and extended in a fan-shaped manner

from the ventrolateral border to the ependymal surface. In some of the microscopic sections there were also a few hemorrhages in the neighbouring brain tissue. These latter hemorrhages were as usually seen well-delimited and not so invasive as those found in the areae postremae, indicating perhaps that the loose structure of the latter might have changed the picture.

INFLAMMATORY REACTIONS

In a survey of neuropathological material from a variety of inflammatory diseases several fairly characteristic pathological reactions were noted. However, since we had access to only a limited number of cases, relatively few generalizations can be made at this time.

A. Acute Bacterial Infections.

In acute bacterial leptomeningitis with only slight subarachnoid exudate the area postrema usually exhibited no important cellular changes other than an increase in mast cells, *e.g.* 13 in one section. In another case of pneumococcal leptomeningitis, where the subarachnoid exudative reaction was moderately intense, there were scattered neutrophilic leucocytes in the area. This was even more striking in a case of pansinusitis, frontal lobe abscess, leptomeningitis and terminal ventricular empyema, Pl. III, Fig. 7. Here the neutrophilic leucocytes were chiefly in the Virchow-Robin spaces of the sinusoids. Fibrin in addition to neutrophilic leucocytes was deposited in the perivascular spaces in another case of acute bacterial leptomeningitis and ventricular empyema, Pl. III, Fig. 8.

In a case of anthrax leptomeningitis with a diffuse sanguino-purulent subarachnoid exudate, arteritis and phlebitis a section which included the area postrema showed normal appearing nerve cells and only a few neutrophilic leucocytes. There were no extravasated red corpuscles. No inflammatory cells were found in other parts of the brain.

B. Tuberculosis.

The areae postremae were affected quite differently in three cases of tuberculosis. The only abnormality in one case of miliary tuberculosis without meningitis or tuberculomas of the nervous system was the presence of scattered lymphocytes and a single mast cell in the areae in question. In another case of generalized tuberculosis and meningitis many of the sinusoids in the areae postremae were surrounded by a broad cuff of lymphocytes and plasma cells. The perivascular exudate appeared to extend from the lateral borders of the areae in question to the subarachnoid space. In a rather marked contrast to this observation relatively few hematogenous cells were demonstrable around the subependymal veins elsewhere, Pl. IV, Fig. 11. There were no multinucleated giant cells, tubercles or diffuse inflammatory reaction.

A quite different reaction was observed in a 4 month old infant who died of miliary tuberculosis with leptomeningitis. In many places the ependymal lining was disrupted by the formation of epithelioid cells, presumably microglial cells and histiocytes, cells which had accumulated in great numbers and had replaced the tissue in the more superficial parts of the area postrema, Pl. IV, Figs. 9 and 10. In the Virchow-Robin spaces there were neutrophile leucocytes, lymphocytes and plasma cells. Ventral to the area postrema several discrete ependymal tubercles similar to the ependymal granulations usually seen in tuberculous leptomeningitis were found. The inflammatory process in the area postrema differed in being more restricted with a lesser tendency to exudation or granulation into the lumen of the ventricle.

C. Syphilis.

Only two cases of neurosyphilis with sections through the area postrema were available. In one of congenital paresis which had been treated with malaria 3 months before death, no changes were found, and there were no treponema in a section stained by the Levaditi method. In the other case of

Lissauer's type of general paresis there was a chronic leptomeningitis, particularly marked around the brain stem. Scattered lymphocytes and plasma cells were seen in the walls of the small vessels and in the Virchow-Robin spaces in the areae postremae. In contrast to other parts of the ventricular walls where a typical granular ependymitis was observed the ependymal lining over the areae postremae had a flat smooth surface.

D. Virus Diseases.

A case of Japanese B encephalitis with a very slight leptomeningitis showed only a slight subependymal infiltrate composed mostly of lymphocytes. There was no evidence of nerve cell destruction or glial reaction of the type which prevailed in other parts of the brain.

In a case of acute anterior poliomyelitis which led to the death of a 15 year old boy on the fourth day of illness lymphocytes, plasma cells and eosinophilic leucocytes were found within the area postrema, Pl. V, Fig. 12. The nerve cells, non-pigmented at this age, were intact. Other notable findings were small numbers of lymphocytes, plasma cells and eosinophilic leucocytes in the leptomeninges and severe destruction of nerve cells and microglial proliferation in the motor nuclei of the medulla. In two other cases of poliomyelitis there were only a few lymphocytes in the perivascular spaces and in the tissue of the area postrema.

E. Post-Infectious Encephalomyelitis.

Two cases of post-measles encephalomyelitis, one case of acute toxic encephalopathy following chickenpox and one case of idiopathic encephalomyelitis were studied. In the two cases of measles no changes of significance could be demonstrated in the areae postremae. In the chickenpox case, a 5 year old child succumbing on the fourth day after the onset of cerebral symptoms, 32 mast cells were found in the Virchow-Robin spaces in three thionine stained sections. In the case of idio-

pathic encephalomyelitis the blood vessels were surrounded by a broad cuff of lymphocytes, all confined to the Virchow-Robin spaces within the areae postremae. The nerve cells in the same regions were unaltered, but between them a few elongated microglial cells resembling "rod cells", could be identified. There were a few "agonal" hemorrhages in the tissue ventrolateral to the areae postremae. Elsewhere, all through the spinal cord, brain stem and cerebrum the characteristic perivenous myelin destruction and microglial reaction was in evidence.

The area postrema appeared to be entirely normal in two cases of multiple sclerosis, one, a 25 year old female who had had symptoms of the disease for four years, and the other, a 68 year old female whose disease was much more chronic.

F. Miscellaneous Infectious Diseases.

In a case of acute infectious polyneuritis and lupus erythematosus discoides a few lymphocytes and neutrophile leucocytes were found in the leptomeninges and in the dorsal parts of the areae postremae. No other lesions could be demonstrated within the nervous system.

In other cases of acute infectious polyneuritis, in cases of lupus erythematosus disseminata, periarteritis nodosa with multiple peripheral nerve involvement, chronic arsenical intoxication, polyneuritis diphtheria and acute idiopathic gastroenteritis the areae postremae had a normal appearance.

TUMORS OF THE FOURTH VENTRICLE

Their Relationship to the Area Postrema.

As stated in the introduction our material was not adequate for a study of hydrocephalus and other disturbances of cerebrospinal fluid circulation as produced by intracranial tumors. In one case of an astrocytoma of the frontal lobes with elevated intracranial pressure, but with little or no dilation of the fourth ventricle and in another case of carcinomatosis of the leptomeninges no significant changes were observed in the

area postrema other than the presence of 4 to 6 mast cells per section.

The possibility of a neoplasm arising from the area postrema is said to have been suggested by Cushing, though we have been unable to trace the reference. In none of the large number of fourth ventricle tumors which have been reported in the medical literature is it clear that the tumor arose in the areae though many obviously have a very close anatomical relationship. In one of our cases dying of adrenal tumor there was an incidental finding of 3 small pedunculated tumors approximately 1.0-3.0 mm. in diameter on the lateral wall of the fourth ventricle and attached to the taenia, Pl. V, Fig. 13. In serial sections it was found that the base of one of the tumors was situated at the rostral pole and dorsal edge of the left area postrema. The tumor was sparsely cellular. The cells were well differentiated with small indented, round or oval-shaped nuclei; and arranged in clusters and, along one edge, in a pallisade. Thick glial fibrils, demonstrated by phosphotungstic acid hematoxylin, formed interlacing bands. No mitotic figures were seen. A moderate number of small blood vessels imparted a somewhat lobulated appearance to the tumor. The tumors were believed to be "astrocytomas" arising in the subependymal region next to the areae postremae. There were no ependymal granulations in the walls of any of the ventricles.

Another case, to be reported elsewhere, was of special interest because a primary malignant melanoma of the leptomeninges was combined with a fibrillary astrocytoma of the fourth ventricle, Pl. VI, Fig. 14. The latter tumor was attached by a broad base to the medial parts of the taeniae from the lateral recesses to the rostral pole of the area postrema. It almost filled the caudal portion of the fourth ventricle with its lateral recesses and extended through the foramen of Magendie, yet did not interfere with the circulation of the cerebrospinal fluid. The tumor had a cellular composition quite similar to that in the previous case. The medulla oblongata was cut in serial sections, and pigmented tumor cells of

the same type as present in the leptomeninges were seen to invade the perisinusoidal spaces of the area postrema. Next to the midline this region contained some isolated atypical highly pigmented cells in its neuropile. The possibility of the malignant melanoma, having had its origin in the pigmented nerve cells of the area postrema was considered. However, the distribution of the tumor cells along the perivascular and perisinusoidal spaces of the area was somewhat more consistent with a secondary extension from the subarachnoid spaces along the vessels.

To the best of our knowledge there is no proven case of a tumor arising from the areae postremae.

SUMMARY AND DISCUSSION OF THE PATHOLOGICAL FINDINGS

From a study of the area postrema in 130 pathological cases which included a heterogeneous group of traumatic, inflammatory, neoplastic and other miscellaneous diseases, the following generalizations are believed to be tenable.

(1) From birth to old age a variety of changes take place. The nerve cells, originally located more at the ventrolateral base, are displaced towards the ependymal surface and their arrangement, at first in small clusters so characteristic of glandular structure, is less apparent at a later age. This tendency of the nerve cells to be grouped and occasionally to appear as double, incompletely divided or multinucleated cells is interpreted as being indicative of continuous cellular division even though mitotic figures are not observed. These observations suggest that a gradual migration of some cells towards the surface might occur all during life.

About the age of 15 years an intracellular granulation, which by specific stains proved to be lipoid, begins to appear in nerve cells. Another pigment, presumably melanin, as identified by its argentophilic property, was present at the age of 25 years. Although subject to rather marked individual variations, the amount of both these substances increases with age. The pro-

portion of pigmented cells near the ependymal surface is greater than in the deep layers. Mast cells were seen at the age as early as 3½ years. Microglia and immature forms of neuroglia which occur beneath the ependyma in early life tend to disappear after a few months, not to return in significant number except in the event of a pathological process. Senile plaques and fibrillary changes were not observed. Based on a few observations no racial differences were detected in regard to the melanin contents of the area postrema.

(2) Ventricular and subarachnoid hemorrhage will within six days result in hemosiderin deposition in the leptomeninges, choroid plexus and, less constantly, the areae postremae. Mast cells are often, though not invariably, increased in number. Trauma of the brain either general as in head injury or local as in puncture of the cisterna magna, may cause petechial hemorrhage (and necrosis) within the areae postremae. "Agonal" hemorrhages are not infrequently observed in or near these areae and owing to the looseness of the tissue are usually more diffuse than in other parts of the nervous system.

(3) Infectious diseases which customarily excite an inflammatory process in the subarachnoid space are attended most commonly at the same time by a similar reaction in the areae postremae. This is usually limited to the perivascular spaces of the sinusoids though at times it may extend all through the tissue, and the infiltrating cells are similar to those in the subarachnoid exudate. A granular ependymitis associated with leptomeningitis seldom, if ever, involves the areae postremae.

The characteristic pathological cerebral changes of neurosyphilis, virus diseases, and post infectious encephalomyelitis and multiple sclerosis do not occur within the areae postremae, and except when leptomeningitis is part of the pathological picture, the same areae appear to be normal.

(4) Within a large group of miscellaneous diseases the areae postremae did not participate in the disease process in a manner that can be demonstrated by usual staining-techniques.

(5) The possibility of neoplasia of the cellular components of the areae postremae is expected, *e.g.* an endothelioma, malignant melanoma, ependymoma or other glial tumors. We do not know of any such cases yet, and in two of our cases the examination of serial sections revealed fourth ventricular tumors which had developed most probably near to, but not in the areae postremae.

CONCLUSION

In general the pathological reactions in the areae postremae are similar to those in the leptomeninges and are quite unlike those which occur in other parts of the nervous system. This is partly to be accounted for by the proximity of these areae to the meninges and the apparent communication along rather wide Virchow-Robin spaces with the subarachnoid space. Other important factors may be the looseness of the tissue, permeability of the blood vessels, and peculiarities in tissue structure. The present study supports the idea that this distinctive anatomical region of the nervous system, whose biological significance is as yet unknown, maintains its unique character in ageing processes and in its reactions to a variety of different diseases.

PLATE I
Figs. 1 and 2.

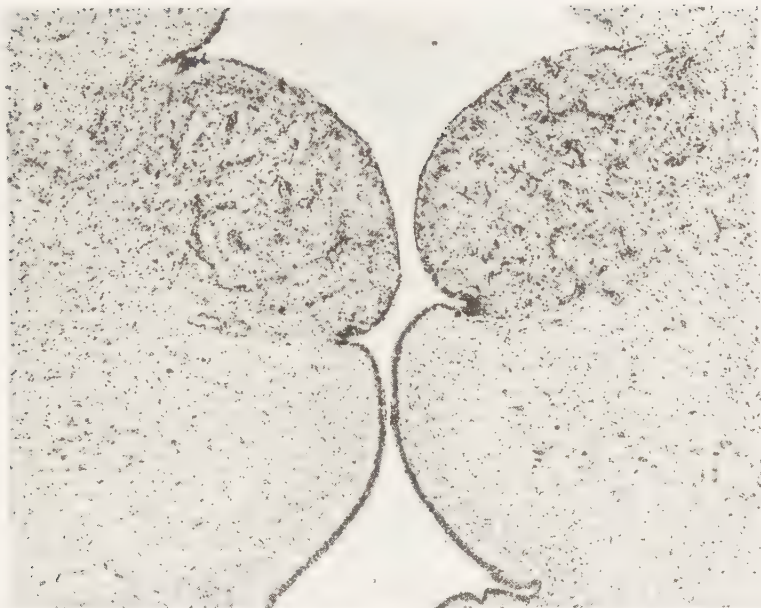


Fig. 1

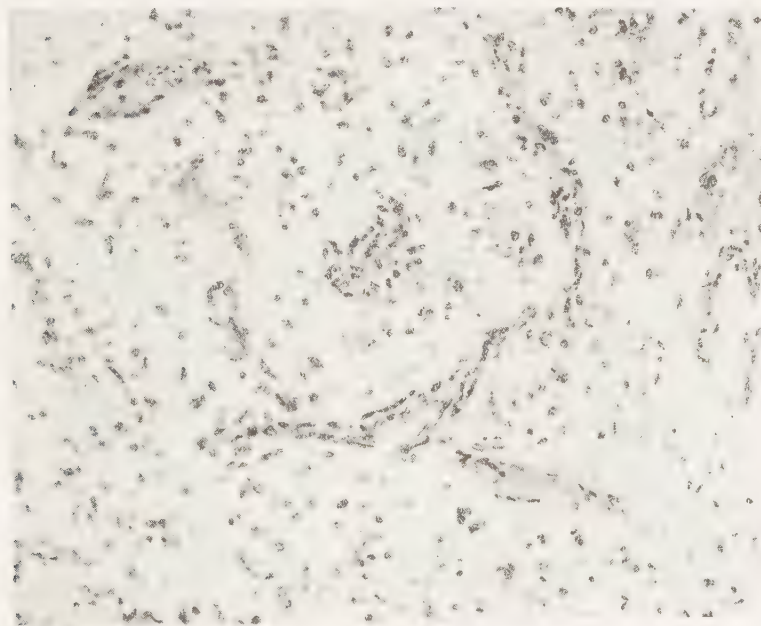


Fig. 2

PLATE II
Figs. 3, 4, 5 and 6.

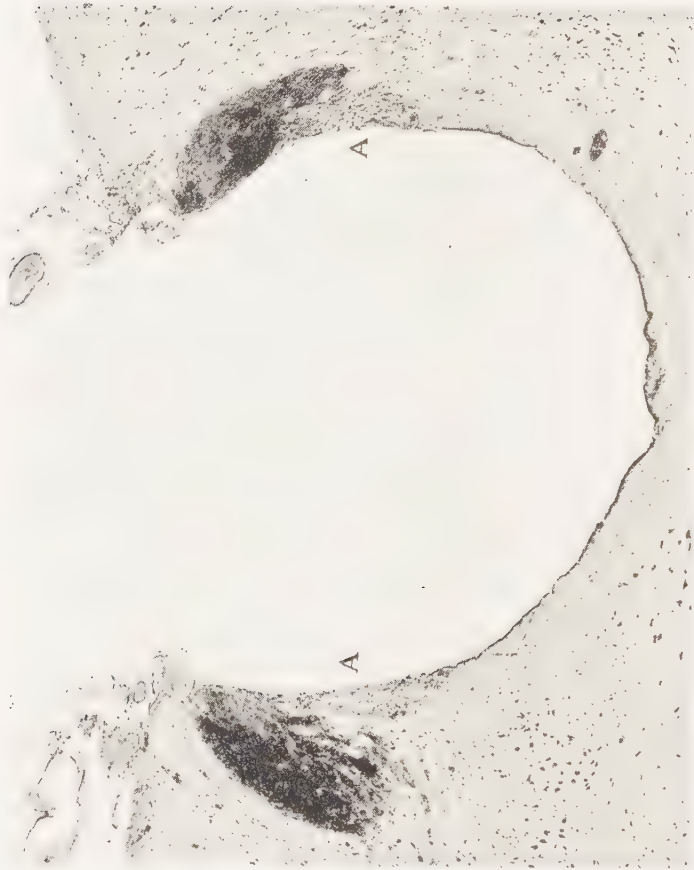


Fig. 6

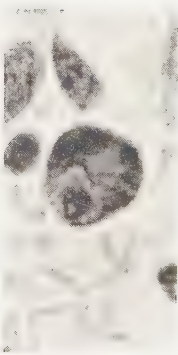


Fig. 3



Fig. 4

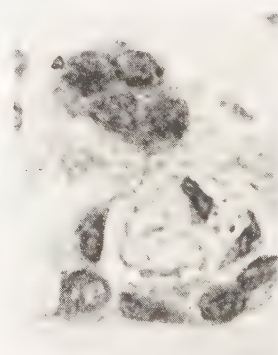


Fig. 5

PLATE III
Figs. 7 and 8.



Fig. 7

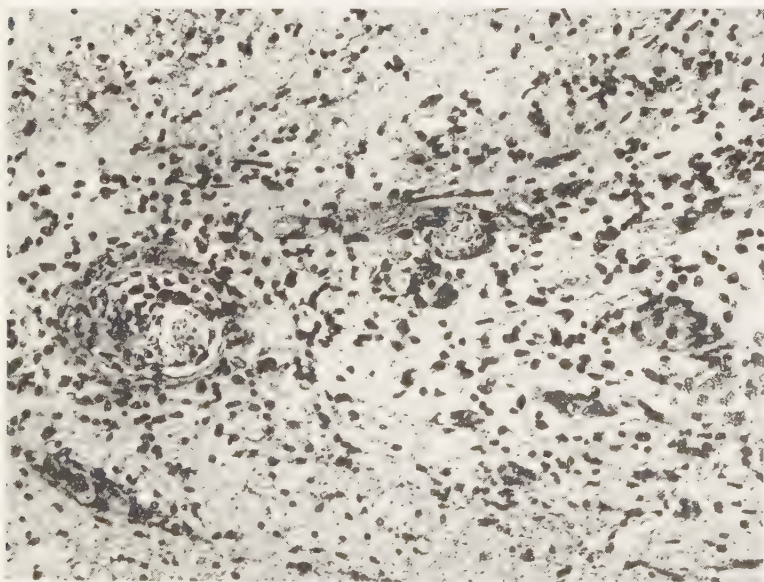


Fig. 8

PLATE IV
Figs. 9, 10 and 11.

Fig. 9

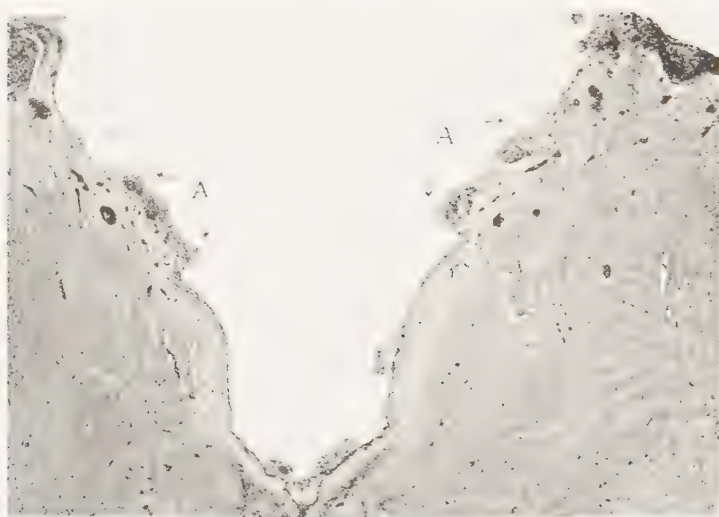


Fig. 10



Fig. 11



PLATE V
Figs. 12 and 13.

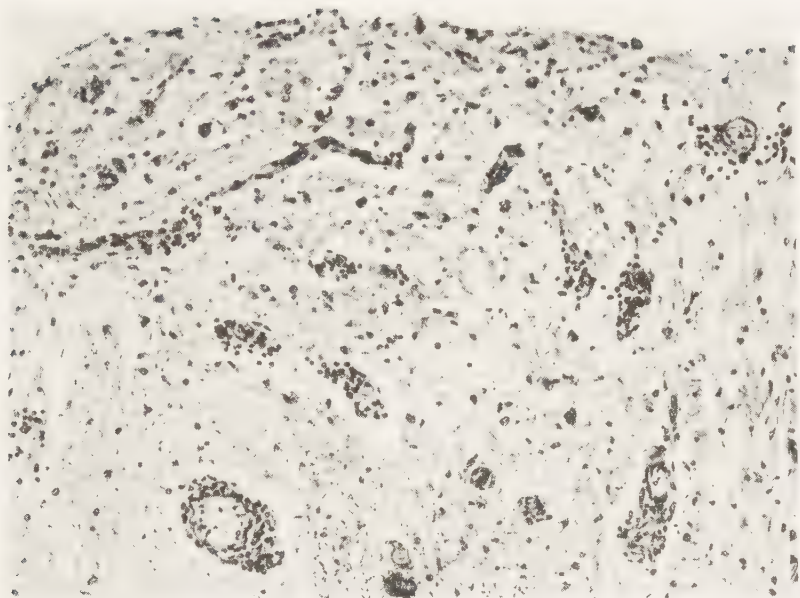


Fig. 12

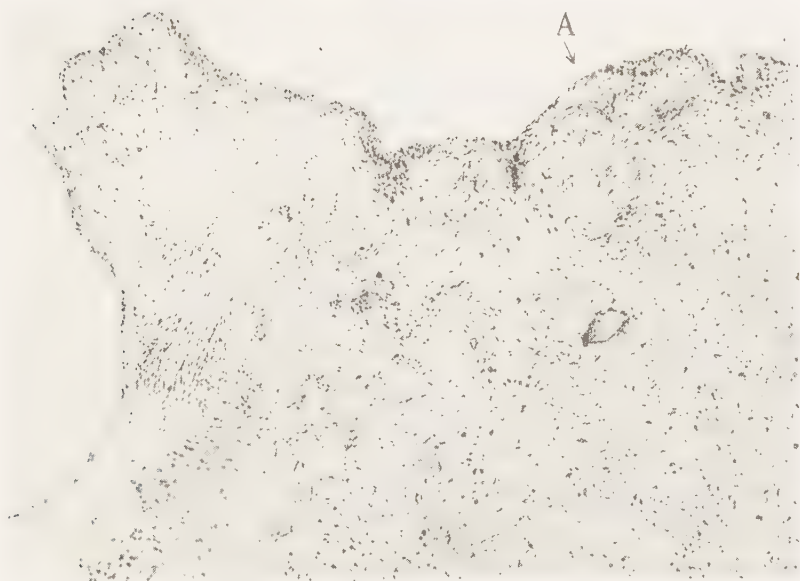


Fig. 13

PLATE VI

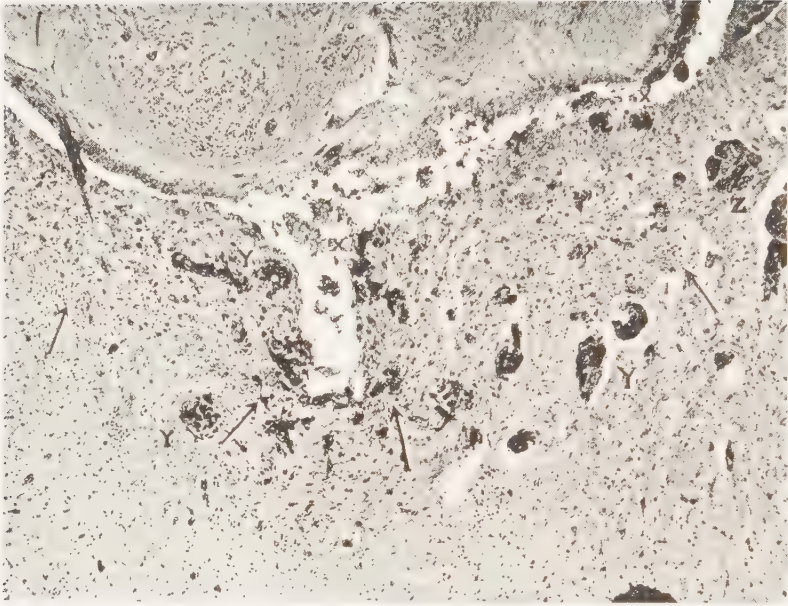
*Fig. 14.**Fig. 14*

PLATE I

Fig. 1:

Area postrema from newborn. The distribution of the vessels gives the tissue a lobulated appearance. A 47-496. Thionine.

Fig. 2:

High-power view of Fig. 1.

PLATE II

Fig. 3:

Faded cytoplasmic "vacuole" next to indented nucleus. Condensation of Nissl substance along periphery of perikaryon. A 47-493. Thionine.

Fig. 4:

Nerve cell with Nissl substance along periphery of perikaryon. A 47-493. Thionine.

Fig. 5:

Multinucleated nerve cell next to sinusoid which is located beneath lining ependyma along the left border. A 47-305. Thionine.

Fig. 6:

Traumatic hemorrhage dissecting the area postrema (A) on each side. Suboccipital cisternal puncture. A 47-417. Thionine.

PLATE III

Fig. 7:

Acute purulent leptomeningitis and localized encephalitis with perivascular leucocyte infiltration chiefly restricted to the area postrema within the medulla. The caudal end of 4th ventricle, the midline irregular cleft, is above delimited by an obex. A 42-681. Thionine.

Fig. 8:

Acute purulent leptomeningitis with moderate diffuse inflammatory process in the area postrema. Darker rings of perivascular fibrin exudation in the upper part of the same region. A 47-207. Hematoxylin-eosin.

PLATE IV

Fig. 9:

Tuberculous leptomeningitis and ependymitis, nodular epithelioid cell reaction and lymphocyte infiltration in the areae postremae. Note the more granular and exudative nature of the process below the areae postremae (A). A. 46-479. Hematoxylin-eosin.

Fig. 10:

High-power view of tubercles in the left area postrema from previous Fig. 9.

Fig. 11:

Tuberculous leptomeningitis with massive perivascular cuffing concentrated in the area postrema (A) and around the vessels running lateral to the tænia of the 4th ventricle and the area in question (B). No. 8769. Hematoxylin-eosin.

PLATE V

Fig. 12:

Acute anterior poliomyelitis with few lymphocytes diffuse in the neuropile and more around the sinusoids of the area postrema and vessels of the adjacent medulla. A 45-350. Thionine.

Fig. 13:

Pedunculated astrocytoma to the left (above) of the area postrema (A). NP 47-30. Thionine.

PLATE VI

Fig. 14:

Primary malignant melanoma of the leptomeninges and astrocytoma, of lobulated structure in the upper part, partly occluding the 4th ventricle (x). Black pigmented tumor cells packed around sinusoids (Y) and vessels (z) lateral to the area postrema (arrows). NP 29-44 (Oslo).

Bodian.

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BLOOD-BRAIN BARRIER IN CONCUSSION

*Remarks on Sten Zetterholm's article on
"Blood-Spinal Fluid Permeability to Bromide in Closed
Head Injuries"*

BY

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In 1939 and in the following years, while engaged in the study of concussion from a different angle, I also examined the blood-brain barrier in 30 cases. Of these, unfortunately, only 18 could be used for my purposes, the rest contained blood in the CSF. It seemed futile to investigate the existence or function of the barrier when an obvious communication existed between blood and CSF, bye-passing the barrier. The number of my cases was too small to permit me to draw definite conclusions or to publish my material, though it was obvious to me that increased permeability of the brain-blood barrier existed in the acute stage of concussion. It is only Zetterholm's article which compels me to publish my findings.

MATERIAL

Out of 30 cases examined 8 were chronic, i.e. the trauma preceded examination by more than 1 year; 22 were acute, and were examined within 4 weeks after injury. Only 10 of the latter group were considered in my account. The age and sex of the cases varied; most of them were middle-aged men.

METHOD

2 methods were used: In half of the cases—acute and chronic— 20 v. cc of 5 % aqueous solution of acid fuchsin were injected intravenously. In the other half of the cases 5 g of fluorescein diluted in a tumbler of water were given by mouth. Lumbar puncture followed 2 hours after the administration of dye. The patient was in the recumbent position. The needle was left in situ and 3-5 cc of CSF were let off at once and, in a few cases, 30 and 60 minutes after lumbar puncture. A few drops of acetic acid were added to the CSF of the fuchsin-tested cases.

It was found by others (Nádor-Nikitits, etc.) and confirmed by me, that no dye appears in the CSF of a normal healthy person under the given experiment conditions. The appearance of fuchsin or fluorescein in the CSF indicates an increased permeability of the blood-brain barrier. The CSF was tested in ultraviolet light for fluorescein whenever there was doubt about its presence.

RESULTS

All 10 acute cases showed and increased permeability of barrier. Dye appeared about 2 hours after intake, in the CSF, irrespective of whether fuchsin s. or fluorescein was given. In those cases in which the CSF was examined repeatedly at intervals, an increase of dye content could be detected in the later portions. No definite opinion could be formed on the optimal time of examination because the dye excretion was not followed up beyond 3 hours after intake.

There was no dye excretion in any of the 8 chronic cases. In one fuchsin-tested case the presence of dye was doubtful. All the chronic cases complained of severe headache of the post-concussional type.

There was only one case in the series which did not suffer from concussion: he was a man of 25 who had a prolapsed disc and sciatica. He was given 3 cc of Lipiodol intrathecally 24 hours before the fluorescein test (5 g. per os at 12.45 p.m.).

Lumbar puncture at 2 p.m.; CSF taken at 2 p.m., 2.50 p.m. and 3.10 p.m. All three portions contained fluorescein. (Increased permeability due to acute inflammation caused by Lipiodol).

COMMENT

It is impossible to draw comparative conclusions between the bromide method on one hand and the fuchsin and fluorescein methods on the other. It would be of interest to apply both methods, bromide and dye, in the same cases simultaneously. If Zetterholm's claim is correct that the presence of blood in the CSF does not interfere seriously with his method then this fact should be a great advantage over the dye methods. The latter being qualitative methods an intact barrier has to be postulated, and since a high proportion of serious concussion cases show blood in their CSF the dye method has to be discarded frequently. On the other hand the simplicity of the dye methods is a great advantage compared with the bromide method.

In my experience *only the acute concussion cases show an increased permeability of the blood-brain barrier*; no dye appeared in the CSF of the chronic cases. This difference is not so clear-cut in Zetterholm's series, though he also noticed the relatively short duration of the "pathological permeability" of the barrier. The difference between his findings and mine is more apparent than real. My cases were either quite acute—1 to 3 weeks after injury—or they sustained concussion 2 to several years previous to examination. The transitory stage was not included in my series, and I am consequently unable to state at what stage of the concussion the increased permeability ceases. The difference between our results is inherent also in the fact that Zetterholm's method is quantitative, while mine is qualitative. In principle our findings are similar.

How far the increased permeability of the barrier is a contributory factor to the sequelae of concussion is hard to say: it is more likely that it will have a prognostic value. About the cause of the increased barrier-permeability one can express

only a tentative opinion: It has been suggested by many authors that the wave caused by the impact on the skull is carried unequally by the CSF and the brain, on account of the different specific gravity of the two substances. One can envisage multiple lacerations in the Virchow-Robin spaces and consequent leakage between blood vessels and the subarachnoid space.

CONCLUSION

An increased permeability of the blood-brain barrier in concussion is confirmed in the acute phase by the fuchsin and fluorescein methods. No increase could be detected in the chronic phase.

The dye methods are simpler than the bromide method, but the latter appears to have a wider application and the to be more precise.

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HISTAMINE AND ANTIHISTAMINE TREATMENT OF HEADACHE PATIENTS

*with Special Reference to
the Therapeutic Action of Histamine*

BY

OLE ESMARCH, M.D.

Knowledge of histamine cephalalgia (*Horton, Mac Lean & Craig*, 1939) and the good results obtained by histamine desensitisation (*Horton*, 1941 and *Dalsgaard-Nielsen*, 1948) have created an interest in the problem of histamine and headache.

In a consideration of the question of histamine and headache it should, however, be kept in mind that experimentally headache may be induced in practically everybody if sufficiently large doses are administered. *Von Storch* (1940) and *Tillgren* (1944), using different techniques, observed that it is easier to induce headache by histamine injections in patients who are regular sufferers from the affection than in healthy people who do not usually have a headache. The headache induced in such patients is as a rule of the same nature as the spontaneous type, and does not display the characteristic syndrome of histamine cephalalgia.

Even though patients with headache of another type are not so sensitive to histamine as patients with histamine headache, the desensitising histamine treatment has shown favourable results in these cases, too. *Horton* (1941) treated 112 patients suffering from headache which could not be regarded as histamine headache in this way. Half of the patients remained unaffected by the treatment, in one fourth alleviation or relief of symptoms was seen for more than 2 months, and in the

remaining one-fourth of the patients the improvement persisted for some length of time, in a few there was even freedom from symptoms for a year. *Tillgren* (1944) treated in a similar way 20 patients in whom subcutaneous injections of histamine in doses of 0.5-1 mg. would induce headache of the same type as spontaneous headache. The patients were divided into groups, and essential improvement was obtained in 1 out of 4 migraine patients, likewise in 1 out of 4 hypertonic persons, and in 7 out of 12 patients in the "general group". No mention is made of an observation period or a later re-examination.

OWN INVESTIGATIONS

The object of the present investigations was to try the therapeutic effect of histamine on a group of slightly susceptible headache patients. In order, if possible, to obtain an insight into the mechanism of the so-called desensitising histamine treatment, the effect of the recently produced anti-histamines on a similar group of patients was observed.

The group of cases which forms the basis of the investigations was chosen chiefly among patients who had suffered from headache for some length of time. No hypertonic persons or cases that might be suspected of histamine cephalalgia or organically conditioned headache were included in the group. The patients were subjected to a thorough examination in accordance with the routine of Danish neurological special departments (*Esmarch*, 1947), and if there was the least cause for it supplementary special examinations were made.

Some patients showed mild simple anemia, myoses, sinusitis or septum deviation. Only after the causal treatment had been terminated and had proved ineffective, was histamine or anti-histamine treatment given. In order to reduce an element of suggestion which may render difficult an estimation of the results, these treatments were not instituted until the patients had been for some time in the department and proved refractory to several of the current methods of treatment.

HISTAMINE-TREATED PATIENTS

A total of 16 patients were treated with histamine, 12 women and 4 men, in whom headache was the dominant symptom in the syndrome. The diagnosis was in one case *traumatis capitis seq.* in another migraine, bronchial asthma, tonsilitis. The central symptom in the syndrome of the other 14 patients was nervousness, the diagnosis being neurasthenia or nervosismus. Only 4 of the patients had been subject to headache for less than a year, while the rest had suffered from it for several years; in 3 cases the symptom had been present for more than 20 years.

The material for the estimation of the effectivity of histamine treatment was purposely made up of cases in which the usual treatments had proved ineffective. With two exceptions several, up to seven, different methods of treatment had been tried, which were more or less directly aimed at the headache.

For the desensitising histamine treatment was used a solution of histamine dihydrochloride of 25 mg.%. The scheme of treatment adhered to was as follows: On the first day 0.2 cc. was administered subcutaneously twice a day, on the second day 0.3 cc. twice a day, and so on up to the ninth day of treatment when a dose of 1.0 cc. twice a day had been arrived at. From the 10th day onward only one injection was given daily, the dose being increased by 0.1 cc. daily till on the 19th day 2 cc. were administered. For the next three days 2 cc. a day were given, whereafter the treatment was regarded as finished.

The initial dose will be 0.05 mg. twice daily, and the final dose will be 0.5 mg. once daily. The doses are somewhat larger than those of *Horton* (1941) and *Tillgren* (1944), who use histamine dihydrochloride and histamine diphosphate, respectively, and who both begin with 0.025 mg. and end with 0.1 mg.

The patients did not know that a new method of treatment was being tried, and the histamine treatment entered as a natural link into the work of the department, the nurses giv-

ing the injections. Questions as to the effects or secondary effects of the cure were of course put quite neutrally.

The first injections rarely cause discomforts to the patients. Gradually as the dose is increased the injection is followed shortly after by headache, flushing of the head or the whole body, and sometimes nausea. The headache coming just after the injections was in all cases—with one exception—of the same character as spontaneous headache. If the injections give rise to a more persistent malaise, a slight reduction may be made in the dose which is then again increased in the usual way. Often, however, the injections must be confined to one a day already from the 5th, 6th, or 7th day of treatment.

12 of the 16 patients showed pronounced improvement under the treatment, stating that there was a noticeable relief of the symptoms as soon as the discomfort after the injection had passed off. In one patient only was the condition aggravated during the histamine desensitisation, so that the treatment had to be broken off when a dose of 1.3 had been reached. In 3 patients there was no improvement during or after the treatment.

At the termination of the treatment there was relief of symptoms in 7 and a marked improvement in 5 patients. Two of the improved patients passed into full health which persisted at the routine control examination a couple of months after termination of the cure. These two patients had only suffered from headache for some few months. A third of the improved patients also passed into complete health and was free from symptoms at the usual re-examination. This patient had suffered from headache for two years, and during two hospitalizations analgetics and sedatives, vitamine B injections, carbon arc light and encephalography (for a combined diagnostic and therapeutic purpose) had no effect on him. The remaining 2 of the improved patients had been treated in the same way without the least effect; gynergen and fever treatment or bellergal had also been tried; their headache had persisted for 21 years and 5 years respectively. After the

histamine treatment there was improvement in one patient for a few days only, in the other for about a month.

Of the 7 patients who were free from symptoms at the termination of the treatment, 3 were in perfect health two months later, their symptoms had persisted from 6 months to 3 years. In the remaining 4 patients the relief of symptoms only lasted about a month. Their headache had persisted for from 1 to 6 years. The patients who were free from symptoms at re-examination had almost all been unaffected by treatment with analgetics and sedatives, aneurin-nicotinic acid injections, carbon arc light, massage, and short wave, sodium bromide given intravenously, or gynergen.

ANTI-HISTAMINE-TREATED PATIENTS

Since alleviation or relief of symptoms is obtained after desensitising histamine treatment of headache patients, it must be of a certain practical and theoretical interest to investigate how such patients react to the recent antihistamine preparations.

The material was chosen in the same way as the above. In all 18 women and 2 men were treated. In the case of 2 of the 20 patients the diagnosis was *traumatis capitis seq.* and in 2 it was migraine-like headache associated with an allergic constitution. In the remaining 16 nervousness was the chief symptom. In 4 patients the headache had given symptoms for less than a year, in the others the affection had lasted for a longer period, in 3 cases for more than 20 years.

Of the synthetic antihistaminic drugs amidryl, which is identical with benadryl, was chosen. When the investigation was started it was the only preparation available, and before it came into the market it was put at our disposal by the courtesy of MEDICINALCO Ltd. Experimentally the substance showed antagonism to histamine, and in man the substance is able to abolish the vasodilatating effect of histamine.

Amidryl was administered in tablets in doses of 50 mg. 3

times a day, the patients being unaware that they were trying a new drug.

Among the 20 headache patients who were treated with amidryl no effect whatever was traceable in 16, and a very uncertain effect in 2. The remaining 2 derived benefit from the treatment. One of them was a neurasthenic, the other an allergically disposed patient with migraine-like headaches. The two patients who were benefited by the amidryl treatment may spontaneously have been in a better period. Nor can a suggestive element perhaps be entirely excluded, seeing that the secondary effects of amidryl in the shape of fatigue, dry mouth, and dizziness may make the patients suspect that they are being treated with an exceptionally strong drug. It is probable that in the case of the allergic patient there may be a specific effect but it must be emphasised that another 3 patients in the group had allergic manifestations in the history without the amidryl having any effect on their headache.

9 of the amidryl-treated patients were later subjected to the usual desensitising to histamine. Of these 4 showed relief of symptoms and 1 amelioration after termination of the treatment. Later re-examination showed that the favourable results persisted in 4. The scanty material must therefore be said to be consistent with the usual observations. It should just be noted that the above-mentioned allergic person was not treated with histamine but preferred continued tablet treatment. The other patient who derived benefit from the amidryl treatment, took histamine treatment and comes under the group of patients with relief of symptoms.

In the histamine treatment of patients who had been pre-treated with amidryl the general impression was that congestions and headache reactions did not set in until doses of 1 cc. or more had been given, whereas in other patients reaction to less than 1 cc. was the rule. This may be due to accidental circumstances owing to the size of the groups, or the pre-treatment with amidryl may somewhat reduce the sensitivity to histamine.

COMMENTS

It must at once be emphasised that the group of patients forming the basis of the investigations on the effect of desensitising histamine treatment on headache is not the best possible if it is desired to obtain positive results. It consisted chiefly of neurasthenic patients who had suffered from headache for years and in whom treatment of other kinds had been ineffective. For technical reasons the treatment with histamine was deferred till the last part of the hospitalisation after other methods had first been tried. That a hospitalisation of some duration will improve neurasthenic patients is beyond doubt. But in the case of patients who have benefited or become free from symptoms it is striking that the desire to be discharged did not arise till after the termination of the histamine treatment when they had the direct impression that the cure had been effective.

It must not be overlooked that an element of suggestion may influence the patients when they are given an extensive treatment with injections which may cause a brief aggravation of the headache, hot flushes, and discomfort. On the other hand excessive importance should not be attached to the suggestive effect if several of the usual methods of treatment have failed and all deliberate suggestion has been avoided during the histamine treatment. It should further be emphasised that nearly all the patients have previously been treated with a score of aneurin-nicotinic acid injections in doses that cause flushing and discomfort of a similar kind. It is true that in the antihistamine treatment the amidryl was administered in the form of tablets, but here, too, there are secondary effects which may perhaps have a suggestive influence on the patients. The negative results here do not prove any greater suggestibility in the selected group of patients and may so far be regarded as a control group in a histamine investigation.

Hence, though the material is scanty, we cannot disregard the essential fact that $\frac{3}{4}$ of the 16 patients showed alleviation

of symptoms during the treatment, and that there was amelioration in 5 and relief of symptoms in 7 at the termination of the histamine treatment. At the later re-examination a couple of months after the treatment there was relief of symptoms in 6, while in 5 patients there was a recurrence in the course of a month and in one already after a few days. The best results were chiefly obtained in patients who had not suffered from headache for a number of years.

The question now arises how the beneficial effect of the so-called histamine desensitisation is to be explained, when a synthetic antihistaminic preparation is practically without effect on a similar group of patients.

At the outset it might be expected that antihistaminic drugs, at least in some degree, would be able to cause an improvement in that type of headache-patients who could be helped by a histamine treatment.

It is, presumably, the general view that the organism is somehow or other desensitised by the histamine injections, but this does not warrant the assumption that administration of synthetic antihistaminic drugs can temporarily in all respects be considered equivalent to a presumed desensitisation.

Ernestene & Banks (1933) point out, however, that there was no evidence of reduced sensitivity to histamine in 13 patients with pruritus, urticaria, and angioneurotic oedema, in half of whom there was alleviation of symptoms at up to 25 histamine injections daily in constant doses of 0.5 mg.

Without taking sides in the lively discussion carried on by allergists concerning histamine and histamine-like substances, we may presumably say that there is still some obscurity and that the antihistaminic drugs have not, as it had been hoped they would, cleared up certain clinical problems.

With regard to headache-patients it must be emphasised that there is something very remarkable in the disproportion between the results of histamine desensitisation and amidryl treatment. Though we would not venture to deny that allergic phenomena may manifest themselves in headache, the ques-

tion nevertheless suggests itself whether there is not in histamine treatment an action on the vessels of the brain.

The most striking effect of histamine is a passing congestion of blood to the head. A similar subjective and objective effect is obtained, however, after intramuscular nicotinic acid injections or intravenous injection of metallosal-manganese. The headache patients, however, did not recover after these treatments, while histamine treatment of the same patients was often effective. This suggests a difference in principle in the effect, and this is further supported by the clinical experience that shortly after the injection of large doses of histamine, employed in the so-called desensitisation treatment, there is an aggravation of the headache, whereas this does not occur after treatment with nicotinic acid or metallosal-manganese.

By clinical experiments *Pickering & Hess* (1932, 1933 & 1939) rendered it probable that headache induced by intravenous injections of histamine was caused by an stretching of the walls of the intracranial arteries and of the immediately adjacent tissue. The headache sets in about 70 seconds after the histamine injection, at a time when the cerebrospinal pressure is again decreasing after an initial rise. *Clark, Hough & Wolff* (1936) state that the headache following the histamine injections is connected with an increase in the amplitude of the intracranial pulsations. The action of an increased arterial blood pressure on dilated cerebral vessels is said to cause expansion and thus pain.

After nicotinic acid injections there will, according to *Moore's* curves (1940), be a more gradual increase in the cerebrospinal pressure, manifesting a hyperemia. In *Dalsgaard-Nielsen's* treatment (1947) of migraine with intravenous metallosal-mangan injections no measurements of the pressure were made. In ophthalmoscopy he had an impression of changes in the retinal vessels; as a rule a minimum contraction of the arteries takes place.

The observations from the histamine injections seem to show unambiguously that fairly massive changes take place in the intracranial vessels. It cannot presumably be quite

improbable that such mechanical influences may contribute to relieve headache without allergic mechanisms coming directly into play.

SUMMARY

On a small group of headache patients who had derived no benefit from the usual methods of treatment a desensitising histamine treatment was tried. Amelioration was obtained in $\frac{3}{4}$ of 16 patients, and at the termination of the treatment there was amelioration in 5 and relief of symptoms in 7 cases. At re-examination a couple of months after termination of treatment there was relief of symptoms in 6 patients, but recurrence of headache after a month in 5 patients, and in one already after a few days.

With practically negative results the effect of an anti-histaminic drug (amidryl = benadryl) was tried on 20 similar headache-patients. 9 of these patients subsequently underwent a histamine treatment with favourable results consistent with the available experience.

Suggestive elements being as far as possible excluded, it may be inferred that there is a fairly good case for improvement in patients with uncharacteristic headache who are treated by repeated histamine injections, through a massive mechanical influence on the intracranial vessels, though it cannot therefore be denied that allergic mechanisms may assert themselves.

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THE ACTION OF HYDROGEN PEROXIDE ON THE UNDAMAGED BRAIN SURFACE

BY

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Hydrogen peroxide is well known and widely used in neurosurgery as an efficient hemostatic agent. It seemed to be of some interest to investigate if its use in any way damaged the brain substance or disturbed the cerebral circulation. As it is difficult in the actual operation to separate the effect produced by the surgical procedure from the action of the hydrogen peroxide some experiments on animals were undertaken.

MATERIAL AND METHODS

Experiments were performed on 9 cats under dial anesthesia (0.1 gr. per kilogram body weight, injected intramuscularly). Through a midline incision the skull was opened with a trephine and the opening enlarged with rongeurs till symmetrical areas of the meninges over the parietal regions of the hemispheres were exposed. The dura was then carefully opened laterally and lifted medially towards the falx so as to uncover the brain surface. A piece of cotton of the same size as the opening and saturated with saline of body temperature was applied to the exposed surface of one of the hemispheres, while cotton, saturated with hydrogen peroxide of the same temperature but varying concentrations (3,5 or 10 per cent.), was applied to the other hemisphere.

After 5 minutes the brain was fixed in situ by injection of 10 per cent. formaldehyde solution through the carotids

after previous short washing of the vessels with saline. The brain was removed immediately and immersed for a few weeks in the fixing solution. In a few experiments the brains were removed unfixed and without washing the blood from the vessels for immersion fixation in 10 per cent. formaldehyde solution to allow a study of the blood vessels through erythrocyte staining *ad modum Sjöstrand* (1934).

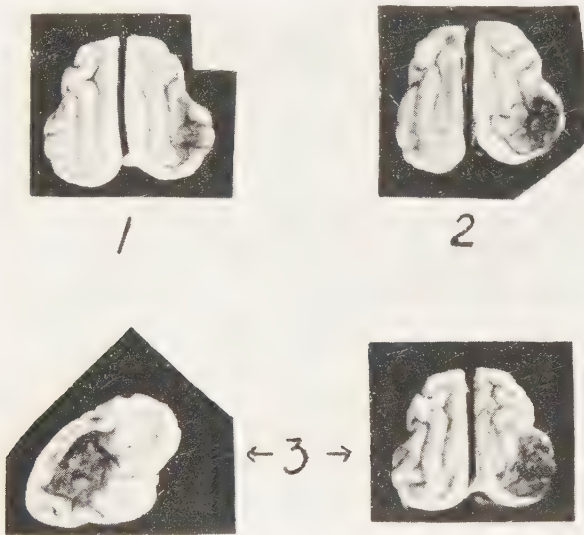
In some experiments the action of the hydrogen peroxide on the blood vessels of the brain was demonstrated by vital staining with trypan-blue. As shown by *Goldman* (1913) and later on e.g. by *Broman* (1940, 1945) the trypan-blue does not penetrate the walls of undamaged cerebral vessels and thus does not stain the normal brain (effect of the so called "blood-brain barrier"). In the case of damage to the vessels, however, the trypan-blue penetrates into and stains the brain substance, leaving a deep blue colour to mark the damaged area when the stain is washed out of the rest of the brain. In the actual experiments with trypan-blue, the hydrogen peroxide was applied in varying concentration in the manner already described, then a few ccs of the 1 per cent. aqueous solution of trypan-blue was injected into the carotids and after one or two minutes the blood was washed out of the vessels with saline and the brain fixed *in situ* as described above.

The fixed brains were embedded in paraffin and sections through both hemispheres stained with hematoxylin-eosin, with toluidine-blue or the Smith-Quigley myelin sheath method. Frozen sections of 100 microns from the brains, fixed only by immersion, were stained for erythrocytes according to *Sjöstrand* (1934).

RESULTS

Some effects on the brain of the hydrogen peroxide were already discernible at inspection of the brain surface during the experiment. The hemisphere treated with saline appeared the same and apparently normal throughout the experiment, whereas the hemisphere treated with hydrogen peroxide showed

some striking changes. Both pial veins and arteries dilated and their diameter increased progressively. This vasodilatation was accompanied by the appearance of many small vessels, which had not been visible before with the naked eye. With a 3 per cent. solution of hydrogen peroxide this effect was present, but was of a moderate degree. With 5 and 10 per cent.

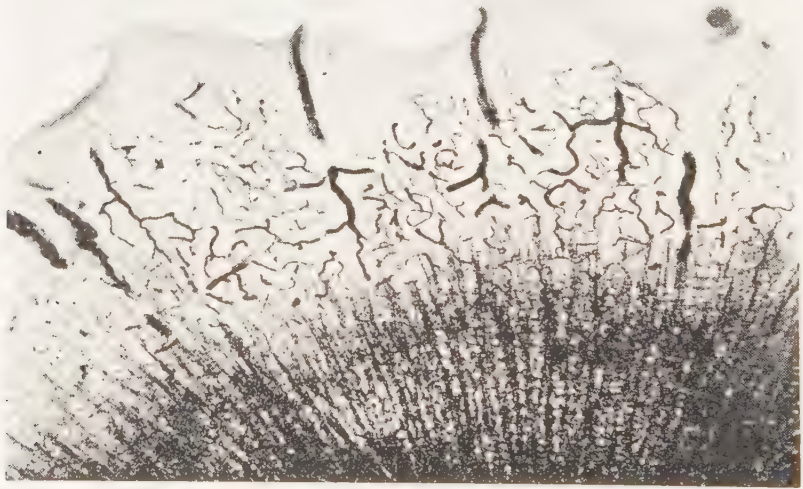


Figs. 1-3.

The area of hydrogen peroxide application appears stained after intravenous injection of trypan-blue. Hydrogen peroxide concentration 3 per cent. in Fig. 1, 5 per cent. in Fig. 2, and 10 per cent. in Fig. 3.

solutions the vasodilatation was more intense in proportion to the strength of the solution. With the highest concentrations small subpial hemorrhages could be seen with a low-power lens. The area treated became markedly oedematous and assumed a pink colour.

When trypan-blue was injected into the blood after hydrogen peroxide had been applied to the brain surface, the area treated showed strong signs of damaged blood vessels in most cases. The area moistened with saline showed no reaction



Figs. 4-5.

Sections through the cerebral cortex of a brain where the vessels have been washed with saline after application of 10 per cent. hydrogen peroxide to the brain surface. Fig. 4 from the normal side: no blood in the vessels. Fig. 5 from the side treated: dilated vessels filled with blood that could not be washed out.—Low magnification. Smith-Quigley method.

at all and only exceptionally an insignificant change. The area treated with hydrogen peroxide acquired a distinct blue colour which spread slowly to the adjoining part of the sur-



Fig. 6.

From the superficial layers of the cerebral cortex in an area treated with a 10 per cent. solution of hydrogen peroxide. Nearly all the cells in a small area are damaged and appear shrunken and show darkish staining. Normal cells on the left.—Toluidine-blue staining.

face, where vessels apparently had not dilated. This effect was rather moderate when a 3 per cent. solution of hydrogen peroxide had been used, but with 5 and 10 per cent. solutions the colour was very pronounced and more so with the stronger

solution (see Figs. 1, 2 and 3). The photographs were taken from fixed specimens, in which the stain is of course preserved in its initial intensity.

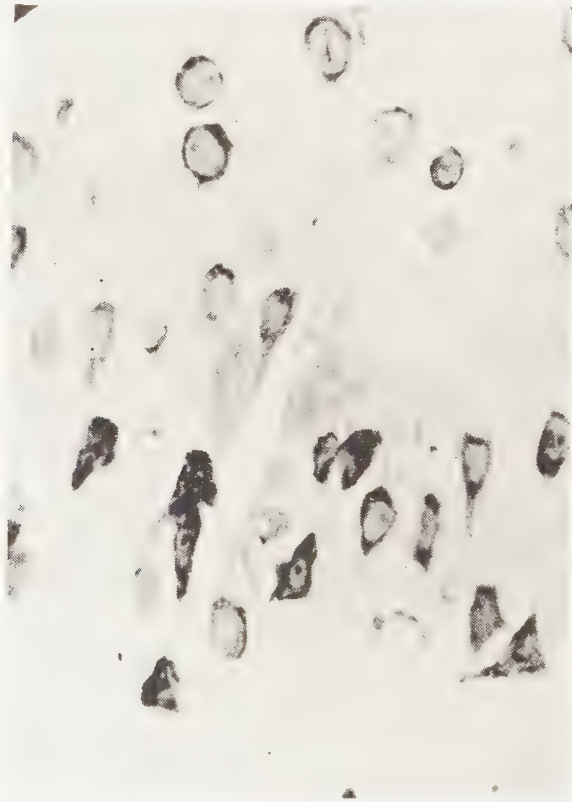


Fig. 7.

Higher magnification of damaged nerve cells. They are shrunken and highly hyperchromatic. Normal cells in the upper part of the picture.—Toluidine-blue staining.

In a few cases small bubbles of gas were seen to be circulating in the veins.

The microscopic examination of the fixed brains showed that the hemisphere treated with saline had the same appearance as in normal animals. The hemispheres treated with

hydrogen peroxide showed some further effects of the treatment. Only those treated with a 10 per cent. solution showed considerable injury. A 5 per cent. solution caused just perceptible injury, while a 3 per cent. solution gave no microscopically visible damage.

The following description applies to the hemispheres treated with a 10 per cent. solution of hydrogen peroxide. In the animals stained with trypan-blue the blue colour penetrated to some depth in the cortex. This might be due to diffusion of the stain from the surface. Other signs of a disturbed circulation under the brain surface were noted, however. Washing out the blood at fixation generally resulted in a very complete emptying of the vessels. In the areas treated, however, patches were seen where dilated vessels were filled with apparently thrombosed blood, which could not be washed out (see Fig. 4). The dilated and stained vessels extended through the grey substance of the cortex. This was never seen elsewhere in the brains.

The nerve cells also showed signs of acute damage below the surface treated with hydrogen peroxide. Diffusely, or in small patches, the cells were shrunken and hyperchromatic (see Figs. 6, 7). This nerve-cell picture is associated with very acute lesions (see *Weil* 1946). In single cells a similar change may be seen here and there in normal areas of the brains, but not to the degree shown here. These brains were fixed *in situ* and thus were not traumatized before fixation. The nerve cells were excellently fixed and stained in other parts of the brains. The nerve cell damage in the hydrogen peroxide treated areas only extended to the superficial layers of the cortex. The patches of damaged nerve cells never went through the whole depth of the grey cortical matter.

DISCUSSION

The result recorded in this paper show that hydrogen peroxide is not quite harmless to the brain tissue. A 3 per cent. solution produced only a moderate dilatation of pial vessels

with a slight and in all probability passing disturbance of their permeability. A 5 per cent. solution had decidedly greater effect in these respects and also affected the nerve cells though only in a small degree. A 10 per cent. solution had a strong effect on the circulation, sometimes even thrombotizing the vessels to some depth in the brain substance. It also caused an unmistakable nerve-cell injury in the superficial layers of the cortex. This graded series of effects is strong additional proof that the damage is really caused by the hydrogen peroxide and not by trauma at the operation or some other accidental factor. Also the control side, treated with saline, showed nothing of the related effects.

The results show that solutions of less than 5 per cent. hydrogen peroxide probably have only passing effects on the brain tissue. A 10 per cent. solution on the other hand causes injuries, which though superficial, are nevertheless serious in their character. It might thus be advisable to use solutions of less than 5 percent hydrogen peroxide for neurosurgical purposes.

SUMMARY

The effect of solutions of hydrogen peroxide of varying concentration on the cat's brain was investigated.

A 10 per cent. solution caused an intense vasodilatation of the pia, probably extending into the depth of the cortex, with markedly increased permeability to trypan-blue. The nerve cells of the superficial cortical layers showed signs of acute injury. A 5 per cent. solution had the same effect, though in a less degree. A 3 per cent. solution caused only changes which in all probability are passing.

It is recommended to use hydrogen peroxide solutions not stronger than 3 per cent. for hemostatic purposes in neurosurgery.

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INTRAVENOUS INSULIN
AS A METHOD TO PRODUCE ABNORMAL
ELECTROENCEPHALOGRAMS
IN EPILEPTICS

BY

HELGE HERTZ and MUNKE HERTEL WULFF

With the introduction of electroencephalography into clinical medicine a method was found to diagnose epilepsy from other paroxysmal diseases even in silent periods. However it was soon found, that not all cases of epilepsy gave the typical electroencephalographic changes, and that there were patients presenting typical epileptic records without having clinical epilepsy. In the McGill studies (*Jasper and Kershman* 1941) it was established, that 5 per cent. of patients presenting clinically typical epilepsy had records within normal limits, even though they were examined repeatedly, and after hyperventilation, 10 per cent. of patients having abnormal records without presenting clinical epilepsy. Apart from hyperventilation other methods have been described to provoke epileptic abnormalities in the records of epileptics with otherwise normal electroencephalograms. *Gibbs* (1947) at the American electroencephalographic congress described the method of recording during natural sleep, or during sleep induced by the barbiturate seconal. (*Gibbs and Gibbs* 1948.)

At the international electroencephalographic congress in London *Baisset Bugnard et al.* (1947) stated that insulin given intravenously, in a dose sufficient to provoke in 20 min. a fall in bloodsugar below 0.50 mg.-per cent., did not affect the records of normal individuals within 30 min., but produced

typical changes in the electroencephalograms of epileptics, in form of bursts of 3-6 cycles waves, also where these were not present before the insulin medication. A longer period of hypoglycemia is known to produce a) a shift of dominant frequency from 8-12 to 6-7 and b) when the state of hypoglycaemic coma is reached continuous waves of 2—3 cycles. (*Berger* (1937), *Hoagland et al.* (1937), *Lennox et al.* (1938), *Gibbs et al.* (1940), *Brazier et al.* (1944), *Heppenstall* (1944), *Engel et al.* (1944) and *Brazier* (1948)). The method of provoking "epileptic" disturbances in the records by hypoglycaemia of short duration was found so promising, that it was at once employed in our departments in Copenhagen. The results have, not, however, been as satisfactory as were hoped. It appears from the results so far that the insulin method cannot be used to distinguish between epileptic records and those of normal subjects.

16 int. units of insulin were given to 18 normal subjects. Of these, 9 were medical students, 2 were physicians and 7 patients with "peripheral" diseases, i.e. fibrositis, prolapsed discs, and peripheral nerve injuries. Bloodsugar and electroencephalogram were taken before the intravenous injection of 16 int. units of insulin, and at intervals of 10, 20 and 30 min. following. The investigation was carried out in the morning and the subjects had been starved since the previous evening.

Of the 18 normal subjects 5 had regular bursts of slow waves 2-5 cycles pr. sec. at bloodsugars: 0.25, 0.41, 0.44, 0.48 and 0.54. None of the five had a family history of epilepsy, or other nervous diseases, nor had they sustained any head-injury. Three subjects (1 with a concussion 1 year previously, 1, whose grandmother had epilepsy and 1, whose mother had migraine) showed records with bursts of 2-3 cycles pr. sec. at a bloodsugar 0.42. In the records of two subjects the dominant frequency dropped to about 6 at bloodsugars 0.70 and 0.23 but both subjects had sustained minor head injuries more than 1 year previously. All the subjects mentioned had a perfectly normal electroencephalogram before insulin was given. It is of note that of 9 healthy students, with an average age

of 20, subjected to the test, 4 reacted with abnormal records. This may be due to increased sensibility of the young brain. Compare the electroencephalographic changes after electroconvulsional therapy, described by *Weil et al.* (41).

The insulin method was further applied to 26 cases suspected of epilepsy but without typical changes in the electroencephalograms. 11 of these patients had typical convulsions, or attacks of petit mal, seen and recorded by the personal in the neurological department. Of these 11, 5 showed typical bursts of slow rhythms 2-4 cycles pr. sec. at bloodsugars between 0.20 and 0.66, but in 4 cases the records were unchanged at bloodsugars between 0.17 and 0.64. Of these four one patient had a family history of epilepsy, one had sustained repeated head injuries, and showed diffuse ventricular dilatation at air encephalograms. One patient had a right sided temporal ependymoma as the cause of her attacks, and one patient showed regular bursts of slow waves in a later electroencephalogram recorded without insulin medication. In one case the bloodsugar did not fall below 0.63, and it was found that the patient had had food previously. Finally in one case with typical convulsions the dominant frequency dropped to 6 from 8-9 cycles pr. sec. at a bloodsugar of 0.30.

The insulin method was tried on 15 patients with various neurological and psychiatric complaints, but with normal electroencephalograms. 8 of these patients showed typical bursts of slow waves, but there was no significant agreement between the results of this method and the clinical diagnosis arrived at, by other examinations. Only two cases of narcoleptic fits were interesting in this respect showing no abnormality in the ordinary electroencephalogram, but with typical bursts of 2-3 cycles, potentials of big amplitude, after insulin medication.

It is the result of this investigations, is that the insulin method in the present form is hardly suitable to demonstrate electroencephalographic abnormalities in epileptics, with otherwise normal electroencephalograms as 4 of 11 patients, with definite epileptic fits, continued to show a normal record after insulin medication, while 5 of 18 normal individuals showed

regular bursts of slow rhythms under the same insulin medication.

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MENTAL SYMPTOMS IN ASSOCIATION WITH PITUITARY-HYPOTHALAMUS LESIONS

BY

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The views advanced in the present paper are based on clinical observations made during my appointment at the Neurological Department of *Frederiksberg Hospital*, to which a considerable number of patients with endocrine diseases are admitted.

I shall first render the case histories of the patients admitted to this department within one year (together with that of a single out-patient) who presented mental symptoms in my opinion referable to a lesion in the hypothalamus. I have divided the patients into 3 groups: I: Patients with pituitary lesion. II: Patients probably with hypothalamus lesion. III: Patients with signs of an organic brain lesion without definite localisation, but presumably affecting the hypothalamus. After the review of the case histories I shall compare my own observations with some statements in the literature.

CASE HISTORIES

GROUP I. Patients with clinically certain pituitary lesion.

1) *F. H. Case 864/46. Unmarried mechanic, aged 25.*

No known predisposition. Previously always in good health, both physically and mentally. His present illness developed insidiously in 1943 with tiredness, torpidity, impairment of memory, headache, and giddiness; moreover, polydipsia and polyuria, as well as considerable

sweating and increase in weight. He has never felt any sexual desire, has never experienced ejaculations, nor had sexual intercourse.

Physical examination: Somewhat coarse features, but not definitely acromegalic, thin growth of beard and scanty axillary hairiness, but remaining growth of hair normal. Considerable increase in weight during stay in hospital, from 78 to 96 kg. (height 180 cm.). Basal metabolic rate low (87 to 90 %). Genitals normal, but a hormone analysis revealed reduced excretion of testis hormone (3 C.U. within 24 hours). Urinary output at times very considerable (2,260 ml. within 24 hours), at the same time low specific gravity (1008). A somewhat low, though not definitely pathological, glucose tolerance curve (once maximally 148 mg.%, and the next time maximally 168 mg.%), indicative of a slightly increased carbohydrate tolerance. Blood pressure somewhat low (100/60). Neurological examination, incl. eye examination, X-ray of skull, and cerebrospinal fluid, showed normal conditions. Ventriculography (June 1945) revealed moderate, diffuse dilatation of both ventricles.

Mentally the patient was previously normal, but has during his illness become emotionally unstable, irritable, hot-tempered, and quarrelsome. In the department his temper was also exceedingly variable. Sometimes he was difficult to please, "hysterical", but in between he was perfectly quiet and decent, and on the whole mentally normal, except for some torpidity.

2) *F. H. Case 70/46. 36-year-old widow of a policeman.*

Two of the patient's sisters suffer from headaches. The patient's physical development had been tardy, while her mental development had been normal. At the age of 12 a slight concussion, after which she began to suffer from migraine-like headaches, which, from 17 to 27 years of age, were attended by palpebral oedema and loss of hair. Present illness: The patient has for the past 10 years or so been suffering from an almost constant, oppressive headache, as well as increasing tiredness and lack of energy, attended by diffuse loss of the hair of the head, particularly over the temporal areas. The past few years she has been in increasingly low spirits (aggravated after her husband's death in a German concentration camp), emotionally unstable, and difficult to get on with.

Physical examination: Looks old for her age, and is somewhat thin (weight 48.5 kg., height 157 cm.). The hair of her head is thin with bald patches. Excretions of gonadotrophin, oestrogen, and androgen very low (less than 5 R.U., 11 M.U., and 0.5 C.U., respectively, within 24 hours). Gynaecological examination revealed a somewhat small uterus. Blood pressure low (95/45). X-ray of the skull disclosed a small pointed osseous projection from the anterior part of the sella, and a minor

calcification over the area of the pituitary body. Neurological examination (incl. cerebrospinal fluid and encephalography), basal metabolic rate, glucose tolerance, urinary output, eye and ear examinations: Normal conditions.

Mentally the patient was very unstable emotionally, egocentric, preposterous, self-willed, and unreasonable.

In January 1946 transplantation of a calf's pituitary was undertaken according to Kylin's method, with intramuscular injection of an emulsion of the ground gland. The patient was submitted to a follow-up examination 18 months later and was found much improved. The headache had decreased and she was more even-tempered. Growth of hair unchanged.

3) *F. H. Case 77/45. Unmarried woman, aged 55 (case history published in Nordisk Medicin 31, 1571, 1946).*

The patient has from childhood presented signs of myxoedema, and has been treated with thyroid until a few years before her admission to this department. She was admitted because of a diffuse arachnitis with transitory neurological signs and symptoms.

Physical examination: Myxodematous appearance. Low basal metabolic rate (64 %), low blood pressure (100/60), small urinary output (ab. 300 ml. within 24 hours), anaemia, and achylia, as well as increased carbohydrate tolerance. The cerebrospinal fluid showed considerable polynuclear pleocytosis and increase of albumin. Radiographically the sella turcica was seen to be considerably dilated (20 × 12 cm.).

Mentally the patient presented at first some torpidity, which, however, subsided under thyroid treatment. But she continued to be emotionally unstable, egocentric, somewhat hard to please, and self-willed, still in between nice and kind.

4) *Legal observant, whom I have submitted to out-patient examination Married telegraph operator, aged 39.*

Mother's brother acromegaly. At the age of 11 the patient had a severe attack of "Spanish influenza". After that he became somewhat reserved, hard to please, and emotionally unstable, but had no particular difficulty in getting on with other people till the development of his present illness. Has previously been punished for larceny. In 1933 suddenly blind of the right eye (amotio retinae), but was otherwise in fairly good health. The patient's present disease came on in 1939 with rapidly developing signs of acromegaly attended by typical physical symptoms. On X-ray examination there was then found considerable dilatation of the sella turcica, but there was no hemianopsia. The patient was given intense X-ray treatment. In 1945 he suddenly developed a severe diabetes mellitus, which soon improved again, however, and transitory signs of diabetes insipidus. The past few years he has been completely impotent.

The patient's psyche has changed entirely since the onset of the disease. He has become very egoistic and exceedingly irritable, but at the same time somewhat torpid.

Physical examination: Appearance typically acromegalic. Had gained considerably in weight, weighing now 99.7 kg. (height 174.5 cm.). X-ray of skull: The sella somewhat less dilated than previously. The blood sugar level was now normal or low, if anything (ab. 85 mg.%), and the blood pressure was low (105/70). His right eye was totally blind. Otherwise normal neurological conditions.

Mentally the patient presented emotional instability with decidedly depressive periods. Moreover, he was irritable, irascible, and impulsive, and probably also somewhat emotionally obtuse.

GROUP II. Young women presenting a characteristic picture, apparently of hypothalamic origin.

5) *F. H. Case 304/46. Unmarried female office clerk, aged 26.*

The patient's half sister suffers from Graves' disease. The patient has had several attacks of influenza, but otherwise previously in good health, both physically and mentally. Menses from the age of 14, regular until her present illness. Was never pregnant. Her present disease came on in 1938, apparently unprovoked, and developed insidiously with increasing headache, giddiness, nausea, vomiting, and fainting fits; furthermore paraesthesia in the fingers, tiredness, and lack of energy, as well as emotional instability, but not proper low spirits. From 1939 her menses became irregular with intervals of up to 3 months. Between 1939 and 1941 she was admitted 6 times to the Neurosurgical Department of the *Rigshospital* because of hypothalamic encephalitis and cerebral atrophy (ventricular type), for which she received 20 X-ray treatments on the pituitary body in 1941. Between 1941 and 1946 admitted 7 times to the Neurological Department of *Frederiksberg Hospital* under a diagnosis of atrophic encephalitis. Her condition improved somewhat with age, but she continued to have fainting fits; was then unconscious for from 15 to 30 minutes with complete amnesia. Also occasionally fairly long periods of amnesia between the fainting fits. Never convulsions. In addition she continued to suffer from headaches and had difficulty in concentrating.

Physical examination: Bodily habitus of the pyknic type, somewhat adipose, with a normal female distribution of fatty tissue, and rather slender extremities. Weight 65 kg. at most (height 158 cm.). Skin and hairiness normal. Neurological examination revealed ptosis as well as absent patellar and Achilles tendon reflexes; otherwise normal conditions. Ventriculography disclosed a huge internal hydrocephalus, including the 3rd ventricle. Cerebrospinal fluid normal. Basal metabolic rate

low (75 to 82 %). Hormone analysis showed reduced excretion of gonadotrophin and oestrogen (less than 5 U. R. and less than 20 M. U., respectively, within 24 hours). Gynaecological examination revealed atrophy of uterus and external genitals. Glucose tolerance normal. Blood pressure low (105/60).

Mentally the patient was inert, despairing, self-pitying, egocentric, "hysterical", but otherwise sweet and kind.

On April 11, 1946 transplantation of a calf's pituitary was undertaken according to Kylin's method. A few hours later she had one of her usual fainting fits, with amnesia for nearly 24 hours. The pituitary transplantation had no unquestionable effect, even though a follow-up examination 18 months later showed the patient's condition much improved.

6) *F. H. Case 262/46. Unmarried female secretary, aged 28.*

The patient's mother is supposed to have had some attacks similar to those of the patient. The patient has had colitis, but no other disease of any note. Was always somewhat nervous, but otherwise she presented nothing abnormal mentally. Menses from the age of 12, regular for a few years, until her present illness began to develop at the age of 14. She put on weight, and a lowered basal metabolic rate was ascertained (ab. 70 %). Has in the course of years been treated with thyroid preparations and other hormone preparations with some effect. The last few years the patient has in addition been suffering from oppressive frontal headache, and she has become emotionally unstable.

Physical examination: Pyknic bodily habitus, somewhat adipose, with normal female distribution of fatty tissue. No myxoedematous signs, skin and hairiness normal. Weight 63 to 61.5 kg. (height 156 cm.). Basal metabolic rate 93 to 94 % (under thyroid treatment). Glucose tolerance curve decidedly low and prolonged (maximally 122 mg.%). Blood pressure normal (125/60). Neurological examination showed normal conditions.

Mentally the patient was unstable, egocentric, troublesome, hard to please, "hysterical", but otherwise rather sweet.

On March 7, 1946 transplantation of a calf's pituitary was undertaken according to Kylin's method, ostensibly with an excellent effect.

When followed up 18 months later she had no headache, was far more stable emotionally, and her menses had become regular. On the whole she was feeling perfectly well, but was still under thyroid treatment.

7) *F. H. Case 239/46. Female medical student, aged 30.*

Her mother suffers from headaches and is often in a depressed mood. A sister of her mother's suffers from Graves' disease. The patient was al-

ways previously in fairly good health. Was perhaps somewhat sensitive, but presented no other mental symptoms of any kind. Menses from the age of 12, previously regular. Her present illness has developed insidiously in the course of the past 3 or 4 years, beginning with an increase in weight and irregular and scanty menses. After some time she developed torpidity with a lacking power of concentration, headaches, in particular premenstrually, and increasing emotional instability. She was easily annoyed, and finally got a "nervous breakdown" while being in for her examination.

Physical examination: Pyknic bodily habitus, somewhat adipose with normal female distribution of fatty tissue. Skin and hairiness normal. Weight 65 to 61.5 kg. (height 160 cm.). Basal metabolic rate low (78 to 88 %). Blood pressure likewise somewhat low (110/60). Neurological examination as well as X-ray of skull showed normal conditions.

Mentally the patient was very unstable, egocentric, preoccupied about her disease, "hysterical", with fainting fits; but she was sweet and kind.

8) *F. H. Case 144/46. Unmarried female warehouse assistant, aged 21.*

The patient's mother suffers from headaches. The patient was previously in fairly good health, both physically and mentally. Menses since the age of 12, always regular. The patient has been suffering from headaches since the age of 14, and has since the age of puberty been somewhat over weight. Both the headache and the obesity have increased the last few years, and she seems at the same time to have become somewhat tired, nervous, and emotionally unstable.

Physical examination: Pyknic bodily habitus, somewhat adipose, with normal female distribution of fatty tissue. Skin and hairiness normal. Weight 68.6 to 66.9 kg. (height 153 cm.). Basal metabolic rate somewhat reduced (88 %). Glucose tolerance curve somewhat low, but not definitely pathological (maximally 148 mg. %). Blood pressure rather low (110/40). Gonadotrophin and oestrogen excretions normal. Neurological examination, including cerebrospinal fluid, showed normal conditions. Encephalography revealed a slightly dilated left inferior horn.

Mentally the patient was sulky and sluggish, probably somewhat self-centred and unstable.

GROUP III. Patients with a moderate, atrophic brain lesion of the ventricular type and peculiar psychomotor attacks.

9) *F. H. Case 518/46. Unmarried domestic servant, aged 21.*

No known predisposition. The patient was previously of normal health both physically and mentally. Intelligent. Present illness: At the age of 16 (in August 1941) the patient fell with her bicycle, but there were

no signs or symptoms of concussion, or on the whole any troubles till ab. a fortnight later. She then began to have fainting fits and to feel tired and sleepy. At first the fainting fits were not attended by convulsions, but lasted 12 to 18 hours. After ab. 18 months the attacks changed in character, now coming on with convulsions, no doubt universal and of ab. 10 minutes' duration, followed by profound sleep for up to several days, after which slow awakening. From 1943 to 1945 the patient was admitted 3 times to the Neurological Department of the *Rigshospital*, where a diagnosis was made of traumatic epilepsy. During her last stay also hysteria and psycho-infantilism were diagnosed. Neurologically a typical Babinski's reflex was found on the right side, possibly also on the left; most pronounced during her first stay in hospital. Encephalography (July 1942) revealed a slightly dilated system without local changes. Otherwise neurologically normal. Mentally the patient was torpid, infantile, and possibly of inferior intellect (I. Q. found to be 85 in July 1942). Otherwise mentally normal.

1945-46 the patient was admitted 4 times to the Neurological Department of *Frederiksberg Hospital* after convulsions; but no fits during her stays in hospital. She was in a state of coma, or nearly so, each time when admitted. After being soporose and somnolent she woke up and became perfectly clear in the course of some days (14 days at most). During the attacks there was constant bladder atony with urinary retention.

Physical examination: The neurological examination showed nothing abnormal. Ventriculography (January 1946) showed marked arachnitis over the areas of the bore-holes, as well as slight dilatation of the ventricular system. The blood sugar level was somewhat low (70 to 82 mg.%), and the blood pressure likewise rather low (110/80).

Mentally the patient was somewhat emotionally unstable between the fits (according to her mother's statement). In the department she was perfectly natural, made no hysterical impression. The nurses characterized her as "the sweetest and nicest girl imaginable".

10) *F. H. Case 407/46. Unmarried pupil for nursing, aged 24.*

No known predisposition. The patient was previously of normal health both physically and mentally. Present illness: In March 1943 the patient had 2 short fainting fits, the cause of which is unknown (yet influenza a few months previously—psychic trauma?), after which followed 8 days of haziness with amnesia for the entire period. After the awakening the patient had an intense occipital headache, diplopia, light *right* hemiparesis, and paraesthesia of *right* upper extremity with dysgraphia (mirror writing). She was admitted to the Neurological Department of the *Rigshospital*, where the diagnosis was one of hysteria, obs. f. sequelae of encephalitis. Was discharged almost completely cured after

2 months. However, the patient has since had numerous attacks of impairment of consciousness. The attacks come on with tiredness, headache, and giddiness, and possibly nausea and vomiting. The next stage is one of torpidity, after which she passes into a state of haziness with clouding of consciousness, possibly hallucinations and motor restlessness. There is amnesia for the entire period. From June 1943 till January 1944 she was admitted 4 times to the Neurosurgical Department of the *Rigshospital* under a diagnosis of atrophic lesion of the *left* hemisphere with hysterical superstructure. In July 1943 ventriculography was undertaken, during which there occurred haemorrhage causing *right* homonymous hemianopsia. In 1944 she was admitted 3 or 4 times to psychiatric departments for "psychogenic episodes".

1945-46 the patient was admitted 4 times to the Neurological Department of *Frederiksberg Hospital* on account of attacks of the above character. On her admission it was impossible to get into touch with her; she seemed to be in pain (headache), and was rather somnolent. When in this condition she was reluctant, refractory, and unreasonable, was generally characterized as "hysterical". She cleared up completely in the course of a few days. Ostensibly somewhat hard to please the first few weeks after an attack, but made a perfectly normal impression in the department, where she was nice and sweet and sociable.

Physical examination: The neurological examination revealed nothing abnormal, apart from right homonymous hemianopsia (developed after ventriculography in July 1943). Glucose tolerance curve high (maximally 250 mg.%). Blood pressure low (100/60). Remaining examinations showed nothing abnormal.

11) *F. H. Case 108/46. Unmarried warehouse assistant, aged 21.*

No known predisposition. The patient has been suffering a great deal from asthma, but was otherwise of fairly good health previously. His relations to his mother were never particularly good. The patient was somewhat hot-tempered, but otherwise he presented nothing abnormal mentally. Present illness: In August 1945 the patient fell with his bicycle; was unconscious and irrational for 24 hours. Was admitted to the surgical department, but was discharged fully restored after 3 weeks. He was now quite well for 10 days, after which he got a convulsive attack. Has since been admitted 3 times to the Neurological Department of *Frederiksberg Hospital* after convulsive attacks, which no doubt each time came on after a conflict with his mother.

While staying in hospital he once had universal epileptiform convulsions, and during his first stay also attacks of considerable motor restlessness, beating the air and kicking, and at the same time hyperventilation. The attacks were reminiscent of hysterical or hypoglycaemic cases,

but the blood sugar level was during one attack 83 mg.%, and glucose had no effect. After the fits the patient was drowsy, remote, and inert for from some hours to a few days. During and after the attacks the patient had difficulty in urinating (bladder atony).

Mentally the patient complained between the attacks of a poor memory; admitted emotional instability and being hot-tempered and irritable. In the department he presented nothing definitely abnormal in a psychic respect between the attacks.

Physical examination: The neurological examination showed nothing abnormal. Ventriculography (October 1945) revealed a slightly dilated, but otherwise normal ventricular system. The glucose tolerance curve was low (maximally 140 mg.%), and the blood pressure was low (almost constantly below 100). The remaining examinations showed nothing particular.

12) *F. H. Case 627/46. Unmarried typographer, aged 23.*

A half-brother mentally ill. The patient in childhood suffered from involuntary urination and was always somewhat nervous, but otherwise normal, both mentally and physically. Present illness: During the years of German occupation the patient took part in resistance work. He was no doubt afraid of being caught by the Germans, saw spies everywhere, and suffered from headaches. In March 1944 he was knocked down by a member of the Schalburg Corps. Is supposed to have been unconscious for about an hour, but then went home. Later in the day he got a violent headache, attended by giddiness and possibly also by a cramped left arm. He lost consciousness again and was admitted to the Neurological Department of *Frederiksberg Hospital*, where he stayed for 20 days only. He was well, apart from a single fainting fit, till May 1945. Has since been suffering from frequent attacks coming on with a feeling of hotness in the head followed by painful twitches in the left side of the face and left extremities, after which he loses consciousness. In the state of unconsciousness there are said to occur universal convulsions lasting for 7 or 8 minutes, after which he is irrational for 5 to 10 minutes. He is tired and has a headache for about one hour after the attack. Ostensibly he feels perfectly well between the fits.

Between July 1945 and August 1946 the patient was admitted 5 times to the Neurological Department of *Frederiksberg Hospital* for such fits. While staying in hospital he had numerous attacks with considerable motor restlessness, during which he rolled about in bed, laying about him. It was then impossible to get into touch with him. Such attacks might last for several days.

Mentally (according to his mother's statement) the patient has since the beginning of his illness become hard to please and unreasonable. He may be impudent and quarrelsome, yet generally only just before

and after the fits. In between he is kind, decent, and sociable. In the department he was likewise very emotionally unstable, but otherwise there were no mental symptoms of any kind; was decent and sociable. Was later admitted to a mental hospital, where he had no attacks nor any mental symptoms.

Physical examination: The neurological examination showed nothing abnormal. Encephalography revealed slight dilatation of the anterior horns, but otherwise normal conditions. Blood pressure somewhat low (100/70). Eye and ear examination, cerebrospinal fluid, X-ray of skull, and electroencephalography showed nothing abnormal.

SUMMARY OF CASE HISTORIES

Group I comprises 4 patients (2 men and 2 women) suffering from clinically certain pituitary lesion with signs of more or less pronounced pituitary insufficiency. In the first case the cause was presumably one of basal encephalitis, in the second the etiology was unknown, the third was no doubt a case of chromophobic adenoma, and the fourth one of eosinophilic adenoma, which at first caused hyperfunction, but gradually presented signs and symptoms of pituitary insufficiency. The endocrine symptoms varied, as dependent on the nature and degree of the lesion, but all the 4 patients presented mental symptoms (though varying in intensity) characterized chiefly by (1) emotional instability, the patients being irritable and irascible, even to the point of explosiveness; (2) egocentricity, the patients being self-centred, self-willed, and difficult to get on with; in short, what people generally call hysterical. Apart from one patient (No. 2), whose pathological condition bore great resemblance to a light case of Simmond's syndrome, all the patients were more or less sluggish, torpid, and somnolent. These symptoms, like certain other signs and symptoms presented by the 3 patients, a.o. obesity, low basal metabolic rate, a tendency to increased carbohydrate tolerance, and low blood pressure, are suggestive of a concurrent lesion of the hypothalamus, which is, therefore, also supposed to be the cause of the emotional instability and the egocentricity.

In group II mention is made of 4 young women whose disease seemed to be localized primarily in the hypothalamus.

In 3 of the cases the etiology was unknown, and nothing neurologically abnormal was found. In the fourth case (No. 5) cerebral atrophy of the ventricular type was demonstrated, probably developed after basal encephalitis. All 4 patients presented a characteristic picture, which seemed identical with that designated as hypogonadism by Bartels & Hjort (see below). They were all between the ages of 18 and 30, somewhat adipose with a normal distribution of fatty tissue. They made no myxoedematous impression; on the whole they had a healthy appearance. All 4 patients had a definitely low basal metabolic rate, and there were signs of hypogonadism with scanty menses in all except one (No. 8), whose case was mild throughout. There was a tendency to increased carbohydrate tolerance as well as to a low blood pressure. They were all troubled with headaches, and 2 of them had fainting fits as well. Characteristic were also their mental symptoms with emotional instability and egocentricity, on account of which they were called hysterical by their associates. None of these 4 patients presented definite signs of a pituitary lesion; but the hypometabolism, presumably also the hypogonadism, and possibly the tendency to increased carbohydrate tolerance and a low blood pressure are suggestive of a lesion of the hypothalamus, which may reasonably be supposed to account also for the headache and the mental symptoms. Clinically the above picture is thus highly reminiscent of adiposogenital dystrophy, which is likewise believed to be due to a hypothalamus lesion. I have also observed similar mental symptoms in a patient with this syndrome.

Group III consists of 4 patients (2 women and 2 men), whose disease manifested itself by peculiar psychomotor attacks. In 3 of them the disease developed after a slight cranial trauma, and in 2 of these the possibility of a psychic trauma cannot be left out of account. In the fourth case (No. 10), the onset did not seem to have a definite cause. In all 4 patients the disease manifested itself by attacks of clouding of consciousness, in 2 of them (Nos. 9 and 10) as soporose periods with no particular motor restlessness of several days'

duration. In the 2 others the clouding of consciousness was attended by motor disturbances, either in the form of universal epileptiform convulsions, or as violent motor restlessness lasting up to several hours (reminiscent of hypoglycaemic attacks). During the attacks it was impossible to get into touch with the patients, and afterwards there was complete amnesia for the periods. Prior to and immediately after the attacks the patients were strange mentally: sulky, snubby, hard to please, quarrelsome, unreasonable, and "hysterical". Between the attacks, on the other hand, they made no "hysterical" impression; were perhaps somewhat emotionally unstable, but kind and friendly, and on the whole quite natural. They all suffered from headaches. Encephalography in all 4 cases revealed a moderately atrophic brain lesion of the ventricular type. Otherwise there were no certain neurological signs or symptoms. All the 4 patients had low blood pressure values, and 2 presented signs of disturbance of the carbohydrate metabolism as well. But none of them showed signs of hypometabolism or hypogonadism; none of them were obese. All the 4 patients have been admitted repeatedly to different neurological and psychiatric departments, where the diagnoses varied between symptomatic epilepsy and hysteria, or both diagnoses simultaneously.

None of the patients of the 3 groups presented any abnormality in a mental respect prior to their present illness. During the illness the patients of the 2 former groups showed mental symptoms of a rather uniform character, manifesting themselves particularly by emotional instability and egocentricity. These patients, therefore, were most often characterized as hysterical by their associates. It seems natural to presume that these mental symptoms are due to a lesion in the vegetative (hormonal?) centres in the hypothalamus. The third group of patients presented mental symptoms of a similar character, but occurring only in attacks. The patients of this latter group were also according to the neuropsychiatric terminology typically hysterical in their form of reaction. However, they all presented signs of a brain lesion

(moderate cerebral atrophy of the ventricular type). To judge from the clinical picture this lesion must be supposed to have affected the pituitary-diencephalic system, notably the hypothalamus, of which also the low blood pressure and the tendency to disturbance in the carbohydrate metabolism is suggestive.

DISCUSSION

Before passing on to a brief review of some of the most important statements in the literature on mental symptoms in association with pituitary and hypothalamus lesions, I shall just mention that recent investigations have shown the existence a very close relationship between the pituitary body and the hypothalamus, both neuro-anatomically and physiologically (4, 10, 11, 15, 16, 17, and 21), so one organ can hardly be affected without this influencing on the function of the other.

As regards pituitary lesions it appears from the literature that conditions of hyperfunction (gigantism, acromegaly, and others) do not seem to be attended by characteristic mental symptoms, at least not such as belong to the sphere of emotions. Frequent symptoms are torpidity and apathy, which, however, no doubt in most cases are due to an underlying tumour (eosinophilic adenoma), possibly affecting the hypothalamus. Conditions of hypofunction, on the other hand (Simmond's syndrome, pituitary emaciation, adiposogenital dystrophy), according to Kylin (15) are far more frequently attended by emotional instability. However, most writers hold that it is only adiposogenital dystrophy that is commonly associated with emotional disturbances; and this disease is now also stated to be due chiefly to a hypothalamus lesion.

Clinically well-characterized hypothalamus lesions have so far been mentioned only comparatively rarely in the literature. But it has long been well-known that the hypothalamus has a great influence on the emotional disposition. This has been demonstrated through clinical observations in patients with lesions in or close to the hypothalamus (tumours, inflamma-

tions, and vascular lesions), as well as experimentally, both on animals and humans (during operations). Yet, the significance of the hypothalamus for the emotional reactions is far from clear. I shall not enter on a discussion of the literature concerning this question, but reference may be made among others to 2 monographs, published recently here in Denmark, by Hermann (14) and Schou (22), where this problem is also dealt with (see further 3 and 10). However, there is reason just to mention that Bartels & Hjorth (2) very recently, on the basis of a series of 50 women, described a characteristic pathological condition which they believe to be a nosological entity, not previously described as such in the literature. They characterize the disease as follows: A previously healthy young woman begins to gain weight, while at the same time her menses become scanty and her libido decreases. The disease is, moreover, associated with different nervous symptoms as well as a lowered basal metabolic rate. Bartels & Hjorth propose the term hypogonadism for this disease, the cause of which, however, they believe to be localized in the pituitary-midbrain system (analogous to adiposogenital dystrophy). This pathological picture seems to correspond fairly closely to that presented by my patients in group II, also with regard to mental symptoms, of which the most important, according to Bartels & Hjorth, are changes of temper (observed in 39 of their 50 patients). The patients are described "as having fluctuating spirits, involving conflicts with their associates, as being liable to crying spells, and feeling constantly indisposed." Dr. Bartels has later told me, however, that his patients were not actually in low spirits, but were emotionally unstable and irascible. Their associates accused them of being hysterical.—There is likewise reason to mention Ostenfeld's investigations (18, 19, and 20) into the incidence of thyroid diseases in association with mental disorders. The results of these investigations are also suggestive that the hypothalamus plays an important part for the emotional affections. Thus, they seem to show a far higher incidence of thyroid diseases among patients with emotional affections

than in the average population. The author presumes that both affections have a common (central) cause localized in the diencephalic-pituitary system.

Finally as regards the possible pathologico-anatomical basis of the hysterical reactions, the literature contains numerous statements from which it seems to appear that some disorder in the diencephalon is responsible for such reactions (5 and 12). Rudolf Brun (5) holds that the hysterical reaction itself is mentally conditioned, but that the release of this reaction requires a predisposition depending on a somatic (congenital or acquired) disorder, i.e. a hypersensitiveness of the hypothalamic centres. This theory seems rather a plausible one, and it likewise seems to explain why the psychic traumas may vary so greatly in intensity. If the predisposing disorder is pronounced, an apparently "hysterical reaction" can be released almost without any psychic insult, whereas if the underlying disorder is inconsiderable, the hysterical reaction is released only by a far stronger psychic trauma.

It is a well-known fact that a predisposition to hysterical reactions may develop after organic brain lesions. This has not infrequently been observed after encephalitis, particularly epidemic encephalitis in childhood. Hysterical syndromes may develop also after cranial traumas, here, too, particularly in children (9 and 23). In these cases the organic lesion seems generally to be localized in the basal portion of the brain, in particular the hypothalamus.

The symptoms of the "autonomic, diencephalic epilepsy" (8) and the "posttraumatic brain stem syndrome" (6), occurring after organic lesions in the diencephalon, are to some extent reminiscent of those observed in our patients of group III. It likewise seems natural to refer to the hypothalamus the organic basis of certain psychopathic types, especially the egocentric, emotionally unstable type (12). The same is possibly the case with dipsomania and certain epileptic and psychogenic episodes. These are, however, still hypothetical theories, which are mentioned only to illustrate the scope of the problem.

CONCLUSION

A rather uniform emotional syndrome seems to have been ascertained on the basis of a number of case histories, partly for patients with pituitary lesions (Group I), and partly for patients with a well-characterized lesion, no doubt of hypothalamic origin (Group II). This syndrome is characterized particularly by emotional instability and egocentricity, symptoms which often cause these patients to be called "hysterical". Although these are frequent mental symptoms, which cannot be said to constitute a characteristic mental picture, they are by no means reminiscent of the preoccupation with themselves and their disease so common among neurotics and patients with diseases running a protracted course. The present series of patients had clinically well-characterized brain lesions, and the mental symptoms are supposed to have been due in both groups to affection of the vegetative (hormonal?) centres in the hypothalamus. A third group of patients, who undoubtedly likewise had or had had an organic brain lesion, presented, after the occurrence of the organic lesion, typically "hysterical" symptoms, suggesting a lesion in the hypothalamus also in these patients.

The material thus bears out the theory of the great importance of the hypothalamus for emotional disturbances and hysterical reactions. Accordingly it will be expedient in such cases also to look for signs of disturbance in the more "somatic" functions of the hypothalamus, among others fat and carbohydrate metabolism, sexual function, and blood pressure.

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A CASE OF GUILLAIN-BARRÉ'S
SYNDROME FOLLOWING VACCINATION
AGAINST SMALLPOX

BY

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Case Report. J. S., a female cook, aged 65. Record no. 1382/47.

The patient had been operated upon in 1928 for gallstone and in 1940 for a cyst in the thyroid gland, but in other respects she had always enjoyed good health. She had not previously been vaccinated against smallpox.

She was born in Sweden, but since 1907 she has been living in New York. As she intended to visit Sweden in May 1947 she had herself inoculated against smallpox on April 19. As there was no reaction on the site of inoculation at the end of one week she was inoculated again on April 26. At the end of April and the beginning of May she felt generally ill and feverish, and had considerable pain and swelling in the left shoulder. She was nevertheless able to continue her work. Around May 2 she began to notice paresthesia and itching in both feet. A few days later her right foot and the toes on the same foot began to feel numb, and her left foot felt slightly weak when she walked on it. She left New York on May 9, feeling fairly well, but the following day she began to feel very ill, with a severe headache and pains in the back, a stiff neck and a moderate rise in temperature. These symptoms abated again during the next few days. On May 12 she began to have difficulty in moving her face. She could not grimace or move her lips. These symptoms from the face as well as the previously mentioned symptoms from the feet persisted during the remainder of the trip.

On her arrival at Gothenburg on May 19, 1947 she was admitted to Sahlgren's Hospital. Her general state of health was then unaffected and she had no headache. Her temperature was normal. At the routine medical examination nothing unusual was found with the exception of a hypertension of 200/100 mm.Hg. On her left shoulder there were two pea-sized wounds, situated close to one another, secreting a little seropurulent

secretion and showing slight inflammation. No other scars after previous vaccinations could be found.

There was no stiffness of the neck, nor was Kernig's sign present. She had difficulty in wrinkling her forehead and could not close her eyelids, the latter feature being more noticeable on the left side. She could not purse her lips and could not bare her teeth at all. There was thus present an almost complete facial paresis of the peripheral type on both sides. There was no paresis of the palate or tongue, and no swallowing difficulties. In the extremities, the flexors of the left elbow joint were a little weak, the pressure of the hand was weaker on the left side, and there was marked paresis of the dorsal flexors in the ankle joint and of the peroneus muscles on the left side. Besides this, there was lowered sensibility in the right foot and for some distance up the leg. The radioperiosteal reflex was weaker on the left side than on the right side. The patellar reflexes were very weak on both sides. The Achilles tendon reflex was weak on both sides, being weaker on the left side than on the right. Babinski's reflex was negative. No spastic phenomena were demonstrable. The state of the reflexes of the abdominal muscles and the abdomen was difficult to ascertain owing to the corpulence of the patient.

Lumbar puncture was carried out on May 20. The cerebrospinal fluid pressure was 6 cm. Nonne reaction ++, total protein 0.71 per mille, 3 cells to 1 mm².

The red and white blood pattern was normal. The sedimentation rate varied from 40 to 60 mm. in 1 hour. The Wassermann reaction was negative both in blood serum and in cerebrospinal fluid.

The patient's neurological symptoms soon subsided. Even as early as June 2 the facial paresis was no longer apparent; there was still a certain amount of weakness in the left foot, however. When she was discharged on June 14 disturbances of the nervous system were no longer demonstrable.

In this case, signs and symptoms of neuritis appeared on both sides of the face, in the left arm and in both legs. Bilateral peripheral paresis of the face is a rare occurrence in connection with the ordinary forms of polyneuritis, but it is comparatively common in Guillain-Barré's syndrome (*Krabbe* (1); *Forster, Brown and Merritt* (2)). The neurological symptoms therefore pointed strongly to this diagnosis. In view of the fact also, that there was a considerable increase in the protein content of the cerebrospinal fluid but no increase in the number of cells, the diagnosis may be regarded as established.

The question then arises whether there was any connection between the vaccination against smallpox which the patient had undergone and her polyneuritis, or whether it was a matter of mere coincidence.

The first symptoms appeared on the thirteenth day after the vaccination; in other words, at a time when, according to general experience, post-vaccinal encephalitis usually begins. This circumstance seems to us to indicate that there was an etiological connection between the vaccination and the patient's neurological symptoms.

We have not been able to find any cases reported, in the extensive literature on the subject of post-vaccinal encephalitis, where the patient presented Guillain-Barré's syndrome. In the majority of the publications, however, certain typical cases have been selected for description, while the vast majority of cases are described very sketchily.

On the other hand, Guillain-Barré's syndrome has been reported as occurring in conjunction with chickenpox (*Schoo* (3)). More and more attention is also being paid to the fact that the syndrome may occur in association with various skin diseases. *Chusid* and *Marquardt* (4), for instance, have described a case in which these symptoms occurred after mustard gas poisoning, and *Bronson* (5) has published a report on their appearance after severe skin disease of varying origin; among his patients he mentions several diphtheria cases. These cases of Guillain-Barré's syndrome following diphtheria diverge in some respects, however, from the syndrome originally described, and it is therefore open to question whether they can really be placed in this disease group (*Delp*, *Sutherland* and *Hashinger* (6); *Gaskell* and *Korb* (7); *Sampson* (8)). *Krabbe* (1) has described cases where the syndrome appeared shortly after immunization against diphtheria, but he considered himself unable to state with certainty whether there was any connection or not. *Andersen* (9), on the other hand, was of opinion that in the cases where he observed Guillain-Barré's syndrome following immunization against diphtheria

it was simply a matter of coincidence. *Dalsgaard-Nielsen* (10), finally, reported a case after a tick bite (*Ixodes ricinus*).

For our part, we consider that the evidence is not sufficiently strong to justify a statement as to whether there is a connection or not; we feel that more cases must be described before the question can be satisfactorily settled.

If, for argument's sake, we assume that there *is* such a connection, two different possibilities are conceivable. Either it is a question of a syndrome, in the picture described by *Guillain* and *Barré*; that is to say, the clinical picture is more or less uniform, but is to be regarded as the organism's way of reacting to different etiological factors. Or else the disease also is etiologically uniform, in which case the different provoking factors would serve to activate a specific virus which had previously been latent in the organism or to prepare the ground for a specific virus supplied from without which would not have had sufficiently favourable conditions for development in the undamaged organism.

Clinical observations may possibly supply the solution to the problem; for the above-mentioned observations, namely that often, after diphtheria, there is a picture diverging considerably from the ordinary forms of diphtheritic polyneuritis and closely resembling the Guillain-Barré syndrome, with polyneuritis and the characteristic cerebrospinal fluid disturbances, but with certain differences as regards the course, to some extent indicate that various types of the syndrome might be distinguishable according to the etiology. This assumption would be still further strengthened if it were proved that in other infectious diseases slightly different types occur according to the nature of the preceding illness. If, on the other hand, the picture should prove to be quite independent of the nature of the preceding disease, then virological examinations would seem to be the only method capable of providing a solution to the problem. Up to the present, however, all such experiments have failed.

Summary. A description of a case in which the patient developed signs and symptoms of the Guillain-Barré type of

disease about two weeks after inoculation against smallpox. The possible connection between the polyneuritis and the inoculation is discussed.

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PERIODICAL DEPRESSION AS AN INDEPENDENT NOSOLOGICAL ENTITY

BY

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On January 19th, 1897, *Carl Lange*, the well-known Danish neurologist, in the Medical Society of Copenhagen read a lecture on the periodical depressions and their origin. He communicated that from his large clientele of the past 12 years a special group of 700 to 800 cases could be separated out which were unlike other depressions or nervous states, such cases as are now called "neuroses". The cases had the chief symptom in common that they displayed melancholy of periodical occurrence, indifference to work and surroundings, a tendency to anxiety and, as more objective symptoms, anorexia and insomnia. The disorder is always cured completely; when the attack is over, there are no traces left of the disease. But it has a tendency to recur, in some cases many times during the patient's life. We do not know the cause of the disease, *Lange* wrote; he himself attached importance to the fact that it seems to occur quite frequently in association with certain forms of arthritis ("uric acid diathesis").¹

The theory of such an auto-intoxication has not been corroborated, and the depressions have not been seen to improve when the forms of diet used in arthritis urica are employed.

¹ Subsequent examinations have not confirmed the existence of any connection between the periodical depressions and the form of arthritis, arthritis urica, in which imbalance of the uric acid metabolism occurs. *Lange* apparently made a wrong estimate of the sediment which is deposited in normal urine allowed to stand overnight.

Like all that has been written by this prudent and discerning physician, his classical description of the periodical depression holds good today, and there was no reason why he should introduce his lecture with apologies for the weak points and defects with which his exposition was encumbered, though, of course, it does not possess the exactitude that is required nowadays in the clinical field.

In Denmark the most noteworthy neurologist of the last generation, *Viggo Christiansen*, had the periodical depression greatly at heart and both in speech and in writing gave a vivid description of how these patients suffer and how much they are misunderstood by their surroundings. The reader is under the impression that *Christiansen* himself must have been familiar with these psychic pangs (2).

In the *Acta psych. et neurol.* 2: 345, 1927, one of the writers (H. I. S.) has last described the periodical depression and added some comments on its history and pathogenesis.

Moreover, *E. Christensen & P. Dickmeiss* have described attempts at treating depressio mentis with gynergen in intravenous injection (3).

In the foreign literature the concept of depressio mentis periodica is seldom met with. See, however, the three small articles mentioned under "Litteratur" in *Neur. Zentralblatt*.

Periodical depression appears to the writers to differ from manic-depressive psychosis in four respects:

- (1) The cyclic course of manic-depressive psychosis is not reproduced in periodical depression, in which manic phases never occur. The mistake almost suggests itself. When the patients recover from a depression, their purely physiological comfort and relief at being freed from anxiety, inhibition and other troublesome symptoms may mimic a slight mania. But there is no mania and none of its characteristic features will develop.
- (2) The hereditary taint is not homologous, i.e. periodical depression does not occur in particular in families with a manic-depressive taint, as will appear from Table 1.
- (3) Determinations of the somatic according to *Kretschmer*,

Max Schmidt and *Strömngren*, suggest that these patients do not belong to the pyknic type as often as the manic-depressive, but more frequently display leptosome features.

(4) The prognosis of periodical depressions differs from that of manic-depressive psychoses.

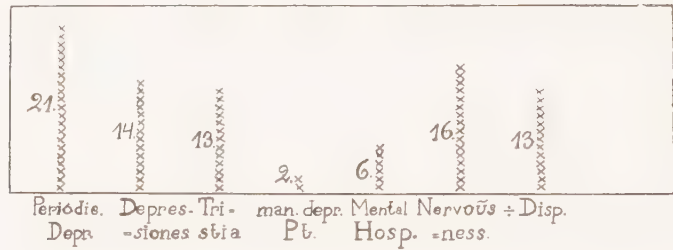
During the depressive phase periodical depression presents exactly the same symptoms as a depression that is a feature of a manic-depressive psychosis: depression, anxiety, inhibition, self-deterioration, lack of initiative, self-reproach, in the case of religious individuals often a certain obtuseness of these sentiments, they are unable to pray and do not get anything out of the service or the Holy Communion. The disorder is often for some time preceded by physical prodromes in the form of obstipation, anorexia and, in particular, insomnia. The course is the usual one, most frequently from three to six months.

Summarizing, it can thus be said: *Periodical depression has no manic phases and differs from manic-depressive psychosis with regard to heredity as well as distribution of somatic types and prognosis.* In the opinion of the writers, periodical depression must thus be considered *an independent nosological entity.*

As was shown in a previous publication (*Ruth Poort: Katamnestiske Undersøgelser over manio-depressive Psykoser, Acta psych. et neurol.* 1945), periodical depression has an especially good prognosis. Only when passing on to the alternating form, a depression or melancholia will get a bad prognosis.

We have examined the cases of depression admitted here in the course of the years 1941 to 1947 under the diagnosis of *depressio mentis periodica*. The total number of patients is 101. The object of the examinations was, if possible, to be able to delimit the periodical depression from the manic-depressive psychosis by means of predisposition and somatic type, also, if possible, by means of the nature, frequency, duration, and prognosis of the attacks. The endogenous depressions were exclusively selected and, as far as possible, it was at-

tempted to leave out the exogenous, psychogenous, depressive reactions. That mistakes may occur is solely due to the fact that, like endogenous melancholia, an endogenous depression may, as is known, both be elicited and aggravated by psychic traumata.



Tabl. I. Familiar disposition i 85 cases of period. depressions.

With regard to *predisposition* it will appear distinctly from Table 1 that in a very great proportion (one third of all patients) there is a predisposition to periodical depressions, in about one fourth there are a few cases of depression in the family, and in one fifth a predisposition to melancholy is stated. But only in two cases a predisposition to manic-depressive psychosis is stated, and this is even doubtful in one case as this patient had not been treated in hospital but was just termed manic-depressive by the practitioner ordering removal to hospital, and the physician who is not a psychiatrist may have used this term to designate a fluctuating frame of mind, depression or melancholy. The other patient has been admitted and treated for mania.

Unfortunately, we have not obtained any information about the diagnoses of the six patients who have been in mental hospitals, except in one case with the diagnosis paranoia hypochondriaca. The other diagnoses may well cloak a depression.

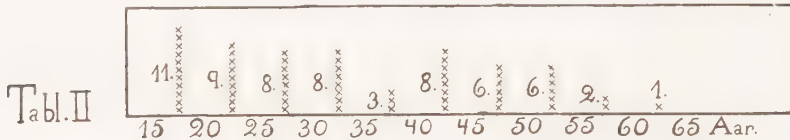
The group "nervousness" does not tell us much. This term would doubtless prove to conceal both light depressions and habitually gloomy temperaments, so that a predisposition to

periodical depressions would become still greater. The same applies to the group "no predisposition". As is known, people are often ashamed to tell that mental disorders run in the family. Insanity is still too often an abusive term among the people. In other cases the patients simply do not know that there is any predisposition. People in general do not analyse themselves or one another to any great extent. If a psychiatrist were allowed to analyse the entire family circle, he would undoubtedly find several divergent cases. But an examination of this nature would require a comprehensive work which would far exceed the bounds of the present small publication. It may, however, be taken for granted that the groups "nervousness" and "no predisposition" do not conceal psychoses, thus in particular no manic-depressive psychoses in this connection. Thus the table shows that a predisposition to manic-depressive psychosis is present in one unquestionable case only. *This is remarkable, considering that almost all psychiatrists include the periodical depressions in manic-depressive psychosis.*

It has not been possible in all these case records, or in the course of the patients' stay in the Nerve Sanatorium, to ascertain any actual manic phase for, if such a phase could have been ascertained, the case would have been classified under the diagnosis of manic-depressive psychosis, but it is a well-known experience that after the attack of depression the patients often have a period of slight exaltation, which, however, can easily be explained as a purely physiological reaction. It goes without saying that a person who feels inhibited, cheerless, unfit for work, sleepless, etc., will feel an enormous relief when this disease subsides, and experience the same happiness as is felt by people after convalescence when they have been suffering from any other disorder, including bodily disorders. What is particularly striking is that patients with periodical endogenous depressions never display psychical deterioration even if the attacks occur ever so frequently during their lives and, as already mentioned, our case records include patients who have had ten or more attacks. In this respect, too, they differ from

the manic-depressive attacks, which, as shown among others by one of the writers (R. P.), in the long run cause both stupefaction and to some extent a change of character, in particular when the attacks of manic-depressive psychosis are numerous and severe.

The *somatic type* has been roughly estimated in 67 cases, an estimate which, of course, must always be super-



Age at the 1st attack in 62 cases of periodic depressions.

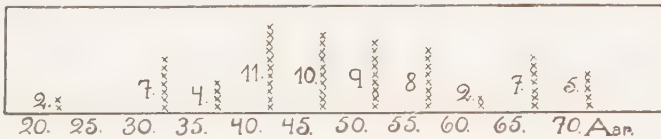
ficial. Further, really useful information is only found in 45 case records, in which 20 are stated to be pyknic or pykniform and, 14 to be leptosome or "nearly leptosome"; lastly, 11 are stated to be of uncharacteristic build.

In 34 cases the somatic type was determined by means of the anthropometric index stated by *E. Strömberg*, in which three measures are used: (I) The height of the body, (II) the width of the chest, (III) the depth of the chest. The measures are transferred to a diagram (one for males, another for females) in which is found a distance which will be the index value. In pyknics the *ab*-point is above the *c*-line, in the leptosome it is below the line. In the measurements performed by us in 34 cases it appeared that the 8 patients were of the pyknic and the 28 of the leptosome build. The figures are, of course, too few to allow of far-reaching conclusions but still the values determined exactly tend in the direction mentioned above, namely that the leptosome type is more frequent than the pyknic one.

The statements about the *premorbid psyche* afford no information of value. 20 patients are stated to be natural, even-tempered, cheerful, 14 of a gloomy disposition, 12 sensitive and apt to worry, 6 nervous, 5 of a fluctuating mood, 2 are

termed isolated temperaments, and 1 patient is termed irrelative. There were no previous attacks pointing in the direction of mania.

Ages at first attack appear from Table II. It will be seen that in a great percentage of cases the disorder sets in before the twentieth year, after which the remaining cases are evenly distributed among the various age-groups.



Tabl. III Age at the last admission to the hospital.

Ages on last admission appear from Table III. This table affords the important information that depression during youthful years is hardly ever hospitalized. This corresponds well with the statements of the patients that during the first years the depressions are generally rare and of short duration, whereas with advancing years they increase both in duration and frequency and also in intensity. Thus only the later attacks will cause the patients to be admitted to hospital.

It has not been possible to render in a table *how frequently the attacks occur*, as many patients state "numerous attacks", which undoubtedly in some cases means attacks recurring almost every year, possibly every second year. In 38 patients we have from 4 to numerous attacks. In 24: 2 or 3 attacks. No regularity can be made out here. We have patients who have been here only once, but who have experienced a number of depressions at home, and we have patients who have been admitted here ten times or more.

The duration of the attacks, as a rule, is only some months, very rarely more than 12 months, as in manic-depressive psychosis. Most frequently it is from 2 to 4-6 or 8 months, in a few cases a couple of weeks only; and only in 2 cases from 2 to 3 years. In this respect, too, the disorder is clearly distinguished from manic-depressive psychosis.

In the following *outline of 102 case records*, the no small number of cases with 5 to 10 attacks of depression are noted in particular. As most of the older cases have been admitted to hospital, a few of them during all the depressions, there is a good and effective control of the nature of the disease. At any rate, they have sought medical advice, possibly from a neurologist, and thus the patient's statements about previous attacks of the disease can be corroborated. In this outline it will be easy to see how frequently there is a homologous predisposition to periodical depression, but it cannot be concluded from the case record whether the depression is of more frequent occurrence in males than in females, as our departments for nervous disorders have more beds for female than for males.

After the outlined case records three more detailed and typical case records follow, which may presumably be read with advantage in full.

With regard to the prognosis, it may be mentioned that the great majority of the patients were discharged as recovered. Thus 31 out of the first 65 patients had recovered completely (i.e. ca. 50 %), 13 had recovered (?), 16 improved, and 5 remained unchanged, but in the two last-mentioned groups there were 3 cases of senile dementia and 7 patients who demanded to be discharged before time and contrary to the advice of the physicians. Compare the prognosis of manic-depressive psychosis with the alternating forms, in which one third were chronic patients and one third were disabled because of frequent and long-standing attacks. With regard to prognosis, too, the periodical depressions thus differ materially from manic-depressive psychosis.

If it is attempted to find descriptions in the foreign literature of the periodical mental depression as a nosological entity, independent of manic-depressive psychosis, the results of one's endeavours will be very poor. It is easily understood that *E. Kraepelin*, the creator of the manic-depressive clinical picture, will not admit that the depression may occur quite independently of manic-depressive fluctuations. He recognizes

that it may nook so, but, like *Thalbitzer*, he maintains that a subsequent slight mania will always occur. It may rightly be supposed that they have misjudged the state of slight exaltation mentioned earlier, which is a purely physiological phenomenon. In the large German collective publication, the *Neurologische Zentralblatt*, we managed to find reports of 4 publications, namely by *Stier*, *Banon*, *Hohman*, and *Speer*, who use the term periodical depression and refer to the disorder as a nosological entity. Most of the authors, however, are only interested in distinguishing between the exogenous and the endogenous depressions—a pursuit which is difficult, because the treatment is quite the same nowadays, namely psychotherapy in the milder cases and treatment with electroshock in the severe cases. None of the four authors, on the other hand, attempts to separate depression from the manic-depressive notion, so that it really looks as if the ingenious physician, *Carl Lange*, has displayed his ingenius here as in other domains.

In conclusion it might be asked—and rightly so—why periodical mental depression has been so little known hitherto, when it has been possible in the course of a period of 6 years to collect about one hundred cases. The explanation is probably a twofold one.

First, all text-books of psychiatry up to the most recent years have been written on the basis of “actual”, i.e. manic-depressive, psychoses. The mental hospitals, or—in the towns—the departments to which the patients are first admitted, have supplied the material used by the authors of text-books, but patients suffering from neuroses in the widest sense of the word or from mild psychoses have for many reasons been unwilling to go to these departments. The strange result hereof is that the professors of internal medicine have seen and described the neuroses, and justly so, because they were the physicians who received and treated these patients. *The psychiatrists of former times never saw neuroses and mild psychoses*, and consequently could not observe periodical mental depression, either. It is characteristic that it was first de-

scribed in Denmark by a professor of pathological anatomy who in addition practised as a neurologist.

The other reason why periodical depression has not previously been differentiated as a nosological entity, independent of manic-depressive psychosis, is that *it may possibly be less frequent in other countries than in Denmark*. When we speak to neurologists from Norway and Sweden, they state that emotional disorders become gradually rarer the higher one gets to the North. On the other hand it is a well-known fact that the mentality of the Danish population is easily moved, so that at any rate the exogenous depressions may grow on rich soil. It may, of course, be by mere accident that the only Danish Nerve Sanatorium up to the present receives such a great number of endogenous depressions, but as our patients come from all parts of the country, and as the percentage of these disorders is found to be almost the same from one year to another, this suggests that we are faced with a fact, namely that periodical depression is a common but hitherto oft-neglected nosological entity, as has been the opinion of one of the authors for about twenty years.

The main object of the present publication is to provide material for reflection and to induce other colleagues in the Scandinavian countries who are engaged in the treatment of the so-called neuroses to test the matter.

SUMMARY OF CASE RECORDS

- (a) means predisposition;
- (b) „ premorbid psyche;
- (c) „ somatic type;
- (d) „ previous attacks;
- (e) „ present attack;
- R. „ recovered;
- I. „ improved;
- U. „ unchanged.

1941

(1) B. P., ♀, aged 42.

(a) No predisposition.

- (b) Prevailing mood even.
 - (c) Leptosome type.
 - (d) 1929 (aged 31) admiss. to hosp.: *Depressio mentis*.
1937 (aged 39) admiss. to hosp.: *Depressio mentis*.
1940 (aged 42) admiss. to hosp.: *Depressio mentis*.
 - (e) 1941 (aged 43) admiss. to hosp.: *Depressio mentis*.
- U. (left against medical advice) Fatigue, low spirits, lack of initiative, not sleeping well, slight self-reproach.
Here, depressed, stagnant, inhibited, apt to isolate herself.—Left sanatorium against advice of physicians. Pentazole shock had been considered.

(2) H. F., ♂, aged 45.

- (a) Father addicted to alcohol.
A maternal aunt has been at the Oringe Ment. Hosp.
Much imbecility in family.
 - (b) Somewhat yielding, irresolute, feeling of insufficiency, isolated temperament.
 - (c) Uncharacteristic build.
- R. (?) (d) From youthful years (14 and 18 years of age), periods of melancholy, ruminating over religion and life, also self-reproach.
- (e) Present depression about 4 months: depressed, anxious, perplexed, self-reproachful.

(3) H. E., ♀, aged 56.

- (a) No predisposition.
 - (b) Always somewhat gloomy.
 - (c) Pyknic.
 - (d) At age of 52 menopause, depression, admitted to private hosp.
 - (e) Present depression of psychical determination (husband's death), been lasting for 11 months in all: depressed, lacking initiative, inhibited, feeling of loneliness. Here, depressed, inhibited.
- R.

(4) K. J. U., ♀, aged 59.

- (a) Paternal grandmother depressed.
- (b)
- (c) Pyknic.
- (d) For the past 10 years periods of depression.
44 years old admiss. Dr. Gulstad's priv. hosp.
53 " " " Dr. Jessen.
54 " " " here for 2 months. Recovered.

(e) 59 „ „ re-admiss. here for 2 months. Ill for
R. Shock, 4. 11 months in all; depressed, sleepless, lacking energy, restless.

(5) N. N., ♂, aged 40.

- (a) A grand-uncle depressed twice.
A grandmother depressed during old age.
- (b) Gloomy, feeling of insufficiency.
- (c) Leptosome.
- (d) At age of 24, a depression for 3 months.

R. (?),
Shock, 7.

- (e) Present depression: about 1 year, depressed, lacking initiative, gloomy, sad, lacking self-confidence.

(6) J. J., ♂, aged 48.

- (a) A sister nervous.
- (b) Somewhat sensitive.
- (c)
- (d) From age of 33, depressive periods of varying duration, with feeling of insufficiency, inclined to isolation, languor, repeated weeping, insomnia.
- (e) Present depression 6 months, with symptoms as above.
Here in a tender mood, somewhat quivering.

R.

(7) D. S., ♀.

- (a) Mother somewhat nervous, of fluctuating mood.
- (b) Sensitive, introvert, ruminative.
- (c)
- (d) 12 years old, depression like the present one; however, not so long-standing and deep.
- (e) Present depression about 6 months; introvert, shy, imperative rumination on metaphysical problems, undefinable anxiety, dejection.
Here, quiet depressed, ruminative.

(8) A. A., ♀, aged 33.

- (a) A brother, aged 21, admitted to ment. dept. of Municip. Hosp. for hypochondriac, paranoid episode.
- (b) Gloomy.
- (c) Pykniform.
- (d) From her 16th year apt to depressive periods, when everything becomes overwhelming and her mind gloomy. 4 or 5 pronounced periods, had to give up work. Once admitted to ment. dept. of Municip. Hosp.

- R. (c) Present depression of indefinite duration.
Here, somewhat weeping, sad, lacking energy.

(9) H. E., ♂, aged 20.

- (a) Father melancholy for periods; also, quick-tempered and obstinate.
- (b) Glad and lively, sensitive.
- (c)
- (d) From his 17th year, a tendency to depressions of short duration: from 1 to 2 to 14 days, with restlessness, uneasiness, irritability, undefinable anxiety, lack of energy, obtuseness of feelings.
Here, of fluctuating mood, chiefly depressed, restless.

I.

(10) L. P. P., ♂, aged 68.

- (a) A brother in ment. hosp. since his 60th year.
- (b) Glad, even-tempered.
- (c)
- (d) 22 years old, a period of depression for 6 months.
- (e) Present depression about 6 months: indisposition, disgust for life, worries, hypochondriac sensations.
Here: depression of senile stamp.

R. (?)

(11) A. L., ♀, aged 72.

- (a) Father periodically depressed about the age of 50.
- (b) Quiet and even-tempered.
- (c)
- (d) Since menopause, at age of 50, often periods of depression and hopelessness, disgust for life, lack of initiative.
To begin with of short duration (3 to 5 months) with similar intervals. Gradually of longer duration.
- (e) Last depression 18 months.
Here, somewhat inhibited, depressed.

(12) A. K., ♀, aged 58.

- (a) No predisposition.
- (b) Always cheerful.
- (c)
- (d) 3 years earlier, a depression for 1 month; no external causation.
- (e) Present depression about 4 months, set in after influenza; sleepless, melancholy, tendency to weeping.

I.

Here, somewhat gloomy, lonely, depressed, tendency to weep, indisposed, fatigued.

(13) N. F., ♂, aged 36.

- (a) No predisposition.
- (b) Always somewhat nervous.
- (c) Big, stout.
- (d) Repeated periods of slight depression with marked sensations of anxiety and low spirits.
- (e) Present depression about 8 months; depressed with anxiety and weeping, hypochondriasis.

R. (?)

Here, depressed, weeping, hypochondriac, feeling of insufficiency.

(14) J. P., ♀, aged 49.

- (a) Mother melancholy, suicide.
- (b) Somewhat fluctuating, at times sad and gloomy.
- (c) Pyknic.
- (d) Since her 31st year attacks of depression, about every second year and of 5 to 6 months' duration; as a rule, in bed for 1 or 2 months.

R.

Admitted here at age of 46: depressed, fatigued, anxious, weeping, indisposed, lacking energy, worried. R.

- (e) Present depression 4 months, exactly like previous ones.

R. (?)

(15) H. C., ♂, aged 49.

- (a) No predisposition.
- (b)
- (c)
- (d) From age of 21 inclined to depressive dejection with irritability and tendency to isolation. Increasing in frequency, in addition associated with consumption of alcohol.

R. (?)

- (e) Present depression several months.

Here, somewhat dull and uninterested, gloomy.

1942

(16) J. L. A., ♂, aged 30.

- (a) A paternal uncle periodically melancholy.
- (b) Natural, cheerful and glad.
- (c) Uncharacteristic type.

- (d) 4 years ago a similar depression for 6 months.
- (e) Present depression 6 months in all: depressed, inhibited, indisposed, lacking energy, not sleeping well, tendency to weeping.

Here, gloomy, sad, inhibited; no delusions.

Shock: R.

Shock (IV): R.

(17) Ø.-H., ♀, aged 29.

- (a) No predisposition.
- (b) Quite natural, active, clever, witty.
- (c) On the pyknic side.
- (d) (1) At age of 21 slightly depressed for a couple of months.
- (2) At age of 28 depressed for 6 months, with attempt at suicide.

Shock: R.

- (3) At age of 29 present depression for about 6 months: gloomy, inhibited, restless, indisposed.

Shock (1): R.

- (4) Since then renewed depression in 1944, about 3 to 4 months: inhibited, lacking initiative, suicidal ideas. Condition suddenly interrupted by father's death. Then, as after all depressions, hypomanic phase, very enterprising.

(18) I. M. J., ♀, aged 22.

- (a) Paternal grandfather melancholy. A sister "nervous breakdown" after over-exertion.
- (b) Quiet temperament, unobtrusive, sensitive.
- (c) Uncharacteristic, on the leptosome side.
- (d) At the age of 17, depressed for a couple of months. At the age of 19, renewed depression for a couple of months, melancholy, fatigued, weeping.

R.

- (e) At the age of 20, depression, now of 18 months' standing: fatigue, low spirits, weeping.

Here, depressed, weeping.

(19) K. S., ♀, aged 43.

- (a) Family nervous.
2 sisters epileptics.
- (b) Inclined to melancholy and speculation.
- (c) Leptosome.
- (d) At the age of 30, a period of insomnia for 1 year, in rest home ("Gl. Skovridergaard"). At the age of 40, depressed for 6 months, since then ill-tempered.

- (c) Present depression 8 months in all; dejection, suicidal ideas.
- R. Here, depressed, inhibited, self-reproachful, despondent.
- (20) A. L., ♀, aged 49.
- (a) Mother depressed, diabetic.
 - (b)
 - (c) On the pykniiform side.
 - (d) At the age of 43, depressed for 9 months, with fatigue. Feeling of reluctance, sad and gloomy mood, inhibition.
- Shock: R. At the age of 46, renewed depression, 5 to 6 months, symptoms as above.
- (e) At the age of 49, depression, 8 months, same symptoms.
- Shock (4): R.
- (21) C. J., ♂ (a joiner).
- (a) No predisposition.
 - (b) Glad and even-tempered, still a little "nervous".
 - (c) Uncharacteristic, on the leptosome side.
 - (d) At the age of 50, depression of psychological determination; admitt. to hosp.
Depressio mentis.
Depressive delusions.
 - (e) Present depression 11 months, fatigued, indisposed, not sleeping well, self-reproachful.
Here, stagnant, lacking initiative, unoccupied.
- Shock: R. Shock (VI): R.
- (22) J. O., ♀, aged 61.
- (a) No predisposition.
 - (b) Previously always in a good humour.
 - (c) Pyknic habit.
 - (d) After menopause about the age of 46, periodical depressions about every other year; to begin with, for a couple of months, gradually longer. Becomes fatigued, slack, gloomy, weeping; headache, paraesthesiac.
- R. (e) Present depression 1 year. Here, depression has practically passed away.
- (23) V. J., ♂, aged 30.
- (a) Mother hot-headed, choleric.

- (b) Fairly good humour, possibly periods of slight exaltation.
 - (c) Pyknic.
 - (d) At age of 28, depressed for about 10 months. Not taking any interest in any things, insomnia, attempt at suicide.
At age of 29, the same.
 - (e) At age of 30, depressed for 5 months; insomnia, slow of comprehension, sluggish memory, feeling of insufficiency.
Shock: R.
Shock (V): R.
- (24) O. H., ♂, aged 42.
- (a) Father melancholy.
A brother 3 times in the Oringe Ment. Hosp. for mania.
 - (b) "Somewhat fluctuating".
 - (c) Uncharacteristic.
 - (d) At age of 30, depression with despondence, fatigue, indisposition, not sleeping well. 1 month.
At age of 31, renewed depression, indisposition, not sleeping well. 1 month.
At age of 38, renewed depression.
 - (e) Present depression 6 months: fatigued, lacking initiative, self-reproachful, not sleeping well.
Here, severe self-reproaches, slow improvement.
- R. (?)
- (25) C. C., ♀, aged 60.
- (a) Mother a great deal depressed from her 50th year until her death 16 years later.
A brother depression twice, suic.
 - (b) Always somewhat "nervous".
 - (c)
 - (d) From age of 40, depression of 1, 2 or 3 months' duration every, or every other, year, preferably in spring.
 - (e) Present depression 3 months: gloomy, fatigued, lacking energy.
- Menopause at age of 46
- R. (?)
- (26) C. J., ♀, aged 42.
- (a) Father periodical depress.
 - (b)
 - (c)
 - (d) At age of 36, after pyelitis grav., depressed, with

suicidal ideas. Mental Hosp., Nykøbing, depress. mentis neurasth. R. Since fluctuating mood.

At age of 39, admitted here for 5 months: depressio mentis. During stay here in fluctuating mood: R. Well-being for 6 months, then again frequent periods with low spirits, not sleeping well, suicidal ideas.

Shock: I.

At age of 42, re-admitted here: depressed, weeping, self-reproachful.

Shock (8): improved.

(27) V. S., ♀, aged 54.

(a) A sister periodically depressed.

(b) Completely natural.

(c)

(d) At age of 51, depression for 3 months; depressed, weeping, poor appetite, loss of weight, not sleeping well.

Menopause at
age of 48

Here, depressed, inhibited. R.

(e) In good health for 18 months, then renewed depression for 8 months, depressed, lacking initiative, not sleeping well, poor appetite, suicidal attempts.

R. (?)

Here, depressed, stagnant, fatigued, inhibited.

(28) E. K., ♀, aged 31.

(a) No predisposition.

(b) "Capricious", but perhaps somewhat sensitive.

(c)

(d) At age of 18, depressed for about 6 months; treated at home.

At age of 24, renewed depression for 1 year; treated at home.

(e) At age of 31, third depression, 14 months, became stagnant, lacking initiative, slack, irresolute, feeling of insufficiency.

Shock: R.

Here, quiet, in a gentle mood, "feeling empty-headed".

Shock (9): R.

(29) V. L., ♀, aged 68.

(a) Father "nervous", reticent, long-standing depress. (psych.).

(b) Uneasy and restless, apt to mind things.

A paternal uncle "nervousness".

- (c)
- Menopause
at age of 49
- (d) From 48 to 50 years of age (menopause) depressed, unfit for work.
From 57 to 59 years of age, renewed depression.
From 64 to 67 years of age renewed depression.
- (e) At age of 68 for 6 months: general feeling of dislike, lacking initiative, fatigued, insomnia.
- R.
- Here, slightly depressed and inhibited.
In completely good health between depressions.
- (30) C. N., ♀, aged 50.
- (a) A paternal uncle melancholy.
A maternal aunt manic-depressive (not treated in hosp.).
A brother depressed for 6 months.
Another brother nervous.
- (b) "Delicate".
- (c)
- (d) Since her youth, periodical depressions.
At age of 22 admitted to the Skodsborg Sanat.
" " " 47 " " hosp. for depression.
" " " 49 re-admitted to hosp. for depress. suic.
Depressed, inhibited, fatigued, sleepless, lacking energy, indisposed, suicidal ideas. No delusions.
Most frequently occurring at Christmas time.
- (e) Present depression 5 months. Here, depressed, inhibited, but already on admission: improvement.
- R. (?)
- (31) I. M., ♀, aged 57.
- (a) A brother nervous.
- (b) For many years nervous, sensitive, pessimistic.
- (c)
- (d) At age of 40, depressed, on leave for 3 months.
At age of 41, renewed depression, on leave for 3 months.
- Menopause
at age of 42
- Not feeling quite well since that time, more sensitive and irritable; periodical aggravation.
- (e) Present depression for 2 to 3 years, of a hypochondriac stamp, snivelling, self-centred.
- R. (?)
- (32) J. C. P., ♂, aged 67.
- (a) A brother suic. (psych.).
- (b) Gloomy.
- (c)

- I. (d) At age of 61, depr. for 6 months. I.
 R. " " " 65, " " 3 " R.
 R. " " " 67, " " 3 " R.
 U. Gloomy, sad, "fed up", religious scruples.
 (Dem. sen.) Here, depressed, worried, hypochondriac.
 Then feeling "extraordinarily well", until,
 (e) at age of 68, depressed for 8 months: depr., despairing, not sleeping well, poor appetite.
 Here, depressed, hypochondriac. Gradually psychotic, with numerous depress. delusions. Unchanged when discharged.
- (33) I. B., ♀, aged 53.
 (a) A paternal uncle depressive in his youth.
 A female cousin (paternal) depress. for periods.
 (b) Normal.
 (c)
 Menopause (d) At age of 33, depressed for 6 months after parturition. Dr. Krabbe.
 at age of 49 At age of 46, depressed for 2 months; in private hosp., Odense.
 At age of 50 (menopause).
 (e) Present depression 1 year: despairing, self-reproachful, with religious rumination, anxious.
 Shock: R. Here, depressed, inhibited, weeping.
 Shock (10): R.
- (34) K. N., ♀, aged 43.
 (a) No predisposition.
 (b) Even-tempered, glad.
 (c)
 (d) (1) At age of 20, depression for 1 year, "fed up", everything was wrong, inclined to weeping.
 (2) At age of 31, renewed depression (after op.).
 (e) (3) Present depression, climacteric, 1 year: depressed, lacking energy, climacteric troubles.
 Here, depressed, inhibited, lacking initiative, somewhat querulous and criticizing.
- (35) A. S., ♂, aged 39.
 (a) Paternal grandmother depressive.
 Father neurasthenic.
 Brother and sister manic-depressive.
 (b) "Emotional person", sensitive, apt to mind things.

(c)

(d) At age of 21, depress.

" " " 26, " , 3 months.

" " " 34, " , 12 "

(e) " " " 38, " , 15 "

Symptoms invariably fatigue, sensations of anxiety, restlessness, weeping, insomnia, lacking concentration.

Here, depressed, seeking consolation; condition very fluctuating.

1943

(36) S. H., ♀, aged 50.

(a) A male cousin feeble-minded. A brother a chronic alcoholic.

(b) Good humour, somewhat emotional, energetic, popular.

(c) Pyknic.

Menopause 2 (d) At age of 43, depression for 3 to 4 months, without years ago; no climacteric troubles cause.

(e) Present depression: set on 1 year ago without external causation. She became sad, cheerless, fatigued, lacking energy, managed work only with difficulty. No depress. delusions.

U. (demanded discharge)

Here, depressed, unable to enjoy anything.

No inhibition.

(37) N. K., ♀, aged 53.

(a) Father suicide.

A paternal aunt and a brother periodical depressions.

A sister's daughter exophthalmic goitre.

(b) Somewhat gloomy, conscientious, without any emotional fluctuations.

(c) Uncharacteristic build, tall, on the leptosome side.

Menopause (d) Since menopause 7 years ago, periodical depressions, in particular in spring and autumn, of increasing duration at age of 46

Shock: R. Appear as fatigue, lack of energy, insomnia, restlessness, unnecessary worry, self-reproach.

(e) Present depression for about 6 months, attempt at suicide.

Here, gloomy, sad, fatigued, lacking energy, reserved, easily moved to tears.
 Shock: R.
 Shock (3): R.

(38) V. W., ♂, aged 48.

- (a) Mother and maternal grandfather nervous.
- (b) "Nervous" during a period of his youth.
- (c) Uncharacteristic type.
- (d) Several times approach to depression.
 At age of 36, depression of 2 to 3 years' duration. Admiss. to the "Hareskov" Sanat., the "Diakonisse-stiftelsen" and here for two years.
 Symptoms: depressed, inhibited, hypochondriac, self-centred, slight self-reproach, "done everything wrong", "my life is wasted".
 Gradually, mostly self-centred.
- (e) Complete well-being for 10 years: then a slight cerebral hemorrhage. Then again depressed, inhibited, unfit for work, sleepless, self-reproachful.
 R. hypochondriac. Duration > 1 year.

(39) E. T., ♀, aged 70.

- (a) A brother has had a depression. During his last years; her father was very cross and melancholy.
- (b)
- (c) Leptosome.
- (d) (1) At age of 59, depression for 7 months: depressed, small fits of anxiety, somewhat dramatic, pitiful, despairing, weeping.
 (2) At age of 66, renewed depression (after complete well-being), 7 months, fatigued, depressed, with insomnia, apt to mind things, despairing; no inhibition, no self-reproach, but worries.
- (Senile dementia)
- I. (e) (3) Then in completely good health till present depression. Now depressed, somewhat whimpering, lamenting in a senile, demented manner, with impairment of memory.

(40) A. V., ♂, aged 59.

- (a) Some "nervousness" in the family. Father easily excited.
- (b) Always somewhat restless, apt to mind things, of an unstable mood, easily excited.
- (c) Uncharacteristic build.

- R. (d) At age of 47, a depression for 6 months, of a nature similar to the present.
- (e) Present depression about 3 years in all. Set in with speculations, insomnia, uneasiness, lack of initiative, fatigue, depression, irritable and unreasonable, possibly of psychic determination (a bad transaction with a farm).
- Shock: R. Here, restless, fatigued, lacking initiative, querulous, cross.
- After shock (V), in completely good health.
- (41) E. R., ♀, aged 49.
- (a) Mother nervous; at age of 36, an "acute attack of mental disorder".
- Admitted to hosp., then in good health.
- Menopause A couple of siblings inclined to melancholy.
- (b) Always somewhat gloomy, sensitive, easily dejected.
- (c) Uncharacteristic type.
- (d) Often dejected for shorter or longer periods. On holiday twice for 6 months. Admitted twice for depression, to hosp. and last to psych. department (aged 26 and 30 years).
- R. (e) Now menopause, depression 1 year.
- Sympt.: sleepless, fatigued, depressed, lacking initiative, general dislike, tendency to weeping, irritability.
- Shock: R. Here, gloomy, depressed, weeping, despondent, no self-reproach, no inhibition.
- Shock (VI): R.
- (42) E. R., ♀, aged 37.
- (a) Father is said to be somewhat like the patient.
- (b) Always been rather apt to mind things.
- (c) Dyscrine.
- (d) Since the age of 17, recurring depressions, with insomnia, restlessness, fatigue, irritability, feeling of oppression on the forehead, pain in the back.
- R. (e) Present depression, 6 months.
- Here, depression now declining.
- (43) E. V., ♀, aged 40.
- (a) During her last years her mother had repeated depressions.
- (b) Somewhat gloomy and sensitive.
- (c) Uncharacteristic.

- Shock: R. (d) At age of 38, depression for 4 months: reserved, silent, distressed, self-reproachful.
Here, sluggish, inhibited, weeping, timid, refusing to eat; self-reproaches.
- Shock: R. Shock: R.—Then in completely good health until
(e) present depression: 3 months in all.
Here, inhibited, perplexed, psychomotor unrest.
Shock: R.

(44) B. H., ♂, aged 45.

- (a) Mother always somewhat melancholy.
A brother has had slight depressions.
- (b) Anxious, over-scrupulous, faltering.
- (c) Pyknic.
- (d) At age of 31, depression for 2 months. Since then, periods of depression of quite short duration, in particular in spring.
- R. (e) Present depression possibly of psych. determination (other conditions of work): depressed, inhibited, lacking initiative, increased doubtfulness. 8 months in all.
- R. Here, gloomy and inhibited, somewhat hypochondriac.

(45) R. K., ♀, aged 40.

- (a) Father repeatedly admitted for depression.
2 paternal uncles epileptics. A sister "has nerves".
- (b) Always in a fluctuating mood.
- (c) Uncharacteristic.
- I. (d) 3 times previously, periods of depression.
At age of 29, depressed for 3 to 4 years (several psych. elements): depressed, suffering, in suspense, with a stamp of anxiety, self-reproachful, self-disparaging, self-centred, self-alluding. Improved when discharged.
- (e) Since then, periods of depression of short duration. Present depression: 3 years in all: depressed, fatigued, not sleeping well, self-reproaches, underestimating herself (again psych. elements, over-exertion, had fallen in love).
Condition fluctuating.
Here, gloomy and sensitive, in suspense, restless.
Shock (V): R.?
- R. (?)

(46) A. V., ♂, aged 70.

- (a) Mother slight attacks of depression.
- (b)
- (c) Pyknic.
- (d) At age of 32, first depression (psych.) of 6 months' duration. During the 15 years that followed, now and again short periods of depression, "fatigued and depressed", was able to work it off. For the next 10 years, repeated attacks of more marked depression, with fatigue, insomnia, lack of energy and depression; duration: about 3 months. Admiss. to hosp. in 1925, 27, 28 and 30. Admiss. here in 1931, 33, 34, 35, 36, 37, 37, 39, 40, 42, 43 and 44.

(47) H. P., ♂, aged 40, born in 1902.

- (a) Family unknown.
- (b) Of a gloomy mood, feeling of inferiority.
- (c) Uncharacteristic build, rather an athlete.
- (d) 4 times admitted to mental hosp. (Oringe) for depressio mentis: in 1934, 35, 36 and 41. Was depressed, weeping, not sleeping well, slightly self-reproachful.
- (e) In 1942 (at age of 40) admitted here; typically endogenous depression: gloomy, sluggish, fatigued, lacking initiative, feeling of insufficiency.

Shock: R.

Shock (IV): R.

One month later, depressed again. Admitted, but demanded discharge.

(48) K. J., ♀, aged 44.

- (a) (1) Father melancholy for periods.
- (2) Paternal aunt very melancholy.
- (3) Father's female cousin 3 times in ment. hosp.
- (4) Female cousin: Depressio mentis.
- (5) A brother in ment. hosp., Nykøbing: neurasthenia.
- (6) Another brother in ment. hosp. "Filadelfia": hypochondria m. gr., paranoia hypochondria.
- (b) Apt to mind things.
- (c)
- (d) Since her youth, repeated attacks of "melancholia", of some months' duration.—During recent years

rarer but, in return, severer and of longer duration, about 6 months.

- I. (e) Last attack > 5 months: depressed, lacking energy and initiative, not sleeping well, a tendency to weeping, inhibition, no delusions.

1944

(49) M. A., ♂, aged 49.

- (a) No predisposition.
 (b) Happy and content, lively, of an easy temper.
 (c) "On the pyknic side".
 (d) (1) In 1939, depression for 6 months: in low spirits, weeping, lacking initiative, sensation of anxiety. Admiss. to ment.: department: weeping, despairing, anxious, self-disparaging, slight sensations.
 (e) (2) Present depression about 6 months; same symptoms, condition worst in the morning, some suicidal ideas. According to statement of his doctor, he was well in the meantime. According to his own statement, not feeling quite well.
- R.

(50) C. J. M., ♂, aged 55.

- (a) Father slight periodical depressions.
 (b) Cheerful and energetic.
 (c) "On the pyknic side", short, strongly built.
 (d) (1) + (2) 10 and 7 years ago, similar depressions of short duration.
 (e) (3) Present depression, about 4 months: restless, depressed, worried, very self-reproachful; worst in the morning.
- R. Here, to begin with, restless, neurasthenic.

(51) A. B. S., ♀, aged 37.

- (a) Father been admitted to hosp. for depression. A paternal aunt admitted here for depression.
 (b) Gentle by nature, tractable, even-tempered, over-sensitive.
 170-28-21½ (c) "A strong, well-nourished pyknic".
 (d) For the past 13 years, relapsing depressions, almost once a year, as a rule in the autumn, generally of 2 or 3 months' duration. The two last attacks
 I. severer than previous ones (simultaneous erotic

(demanded conflict). Depression, fits of weeping, sleepless,
discharge) lacking capacity for work, vegetative symptoms.
Here, when admitted, quiet, gloomy, reserved.

(52) B. C., ♀, aged 65.

- (a) Father very gloomy.
A sister and a paternal aunt nervous.
- (b) Always inclined to depression of a few days' duration.
- (c) "Rather of a pyknic type".
- (d) As mentioned above, always inclined to depression of a few days' duration, with uneasiness, restlessness, weeping. Increasing for the past 6 or 7 years (feeling more lonely). Admitted four times for depression to the Stege Hosp.

(demanded (e) Present depression, about 6 months: depressed, lack-
discharge) ing energy, weeping, irritable.

Here, gloomy, depressed, stagnant, easily tears in her eyes.

Improved, but not well when discharged.

(53) J. T., ♀, Aarhus, aged 53.

- (a) Father somewhat nervous, erethetic.
- (b) Natural, even-tempered, cheerful.
- (c) Pykniform.
- (d) For the past 12 to 13 years, inclined to depressive dejection without any external causation. Increasing in frequency and duration with advancing years, being resistant particularly now in the climacteric, this manifesting itself as a state of general dislike, fatigue, disinclination, a tendency to isolation, lack of initiative and of power of concentration.

Shock: U.

Here, gloomy, weeping, despondent, slight feeling of insufficiency. No real effect of shock treatment. No spontaneous improvement.

(54) E. N., ♀, aged 34.

- (a) Paternal grandfather, depressive psychosis.
Paternal grandmother, depressive psychosis, suic.
Paternal uncle, suic., nervousness, blind.
- (b) Quiet, serious, religious.
- (c) Leptosome type.
- (d) At age of 23, depression with religious worry and self-reproach. 6 months in Ment. Hosp., Nykøbing, R. In good health for 10 years.

At age of 33, renewed depression, 2 months, symptoms as now.

- I. (e) Present depression, 3 months: sad, gloomy, irritable, over-sensitive, worst in the morning.
Here, gloomy, sad, weeping, demanded discharge.

(55) M. J., ♀, aged 57.

- (a) Mother periodically depressed.
Maternal aunt in ment. hosp.
A sister's son, dementia præcox?
- (b) "Of an unstable mood".
- (c) Pykniiform.
- (d) First depression in 1927 (aged 40), treated in Dr. Viggo Christiansen's private hospital. Since then repeated admiss. to hosp. for depression. In the psych. department of the Frederiksberg Hosp. and at "Filadelfia" (here ten times). Fatigued, gloomy, despondent, lacking energy. Now and again also approaching psychosis, misinterpreting, self-alluding, restless. Gradually much absorbed by her disease.
- I.

(56) C. C., ♂, (a clergyman), aged 70.

- (a) No predisposition, the family of a bright temper by nature.
- (b) Natural, lively, cheerful.
- (c) Pyknic.
- (d) Already during youthful years, depressive periods, which have increased with advancing years because of his physical disease (spastic spinal paralysis). Admitted here at the age of 60: depressed, silent, anxious, restless, abandoned by God, everything is overwhelming, hopeless, of the blackest dye.
- (e) Since then only slight approaches until present depression which seems to be of psychical determination. Depressed, gloomy, feeling superfluous, much worry.
Here, gloomy, desperate, with hypochondriac absorption in obstipation.
- R. (?) The depression subsided gradually.

(57) K. K., ♀, aged 53.

- (a) Paternal grandmother periodically depressed.
- (b) Since puberty depressed for periods.
- (c) Of asthenic habit, leptosome.

- (d) The periodical depressions, of 1 to 2 months' duration at intervals from 2 weeks to several months, manifested themselves as self-reproach, ideas of inferiority, self-accusation, auditory hallucinations. A single depression 8 months.
Recent depressions more frequent.
- U. Here, gloomy, sad, stagnant, mostly in the morning, distressed and unhappy, weeping.
- (58) E. E., ♂, aged 68.
- (a) Mother and maternal grandfather periodical depressions.
A brother 2 months in Ment. Hosp., Nykøbing: depr. ment. hypochond. præsenilis?
A more distant relation of his mother's suic.
- (b) "Always" melancholy.
- (c)
- (d) Since age of 25, periodical depressions of 1 or 2 months' duration at intervals of some years. Last attack 5 months. Is gloomy, sad, insufficient for work, lacking spirit and energy.
- I. (?) Here, gloomy, of an aged appearance.
(demanded discharge) Soon demanded discharge.
- (59) V. S., ♀, aged 56.
- (a) A sister periodically depressed.
A brother feeble-minded.
- (b) Psychically natural; however, always quiet.
- 149-26½-18 (c) On the pyknic side.
- Index: —0.2. (d) (1) At age of 50 depressed without any external causation, weeping, poor appetite, loss of weight, not sleeping well. 1½ months at "Filadelfia".
Aged 50. Depressed, inhibited, rapid improvement.
- R. (2) Then complete well-being for 1 year, followed by renewed depression, sleepless, ruminating, attempting suicide.
- Aged 52 (3) Then complete well-being for 2 years. But again depressed, dejected, no zest for life, poor appetite. Here for 2 months: stagnant, with a stamp of anxiety, silent.
- R. (?) Demanded discharge.
- I. (demanded discharge)

(60) D. J., ♀, aged 51.

- (a) A female cousin has been in the Risskov Ment. Hosp. for melancholia for 6 months, recovered. Mother nervous, sensitive.
- (b) Gloomy, sensitive, inclined to dejection.
- (c) Uncharacteristic, short.
- (d) (1) At age of 15.
(2) At age of 20, depression with self-reproach and ideas of inferiority.—Since then approach to depression.
- (e) (3) Present depression about 1 year: indefinite mood, slight inhibition, not sleeping well, irritability. Here for 4 months: gloomy, sad, of indefinite mood, slightly inhibited, slow improvement.

R.

(61) A. C., ♂, aged 41.

- (a) Father and paternal uncle, periodical depressions.
- (b) Somewhat sensitive and apt to mind things, lively, active.
- (c) Lean, slender, leptosome.
- (d) Since puberty, periodical depressions, to begin with at intervals of several years, of 2 to 6 weeks' duration. Gradually more frequent, about every second year, of 2 to 6 months' duration. In particular in spring and summer. Is then dejected, weeping, lacking initiative, irresolute, self-reproachful; worst in the morning.
Present depression 5 months. Here, gloomy, weeping, slightly inhibited, slightly self-reproachful.

I.

(62) E. H., ♀, aged 74.

- (a) Father melancholy. A sister nervous. A niece died in ment. hosp.
- (b) Sensitive, but lively, high spirits.
- (c)

- R. (d) (1) First depression at menopause, 42 years of age, in Prof. Daniel Jacobson's private hospital. R.
- R. (2) At age of 61, renewed depression, admiss. to "Ebenezer".
- R. (3) At age of 65, renewed depression, admiss. to St. Josef's Hosp.
- R. (4) At age of 67, renewed depression, admiss. to "Filadelfia", 2 months. Depression for 5 months

in all: depressed, anxious, religious scruples, self-reproach, is weeping, dispirited, restless, timid, sleepless. Admiss. to psych. department of University Hosp.; transferred to "Filadelfia". Rapid improvement here.

- R. (5) At age of 68: in completely good health since last admiss. Then renewed depression, admiss. to "Filadelfia", sleepless, weeping. Rapid improvement here.
- (6) Since then a depression almost once a year, when she feels dejected and superfluous, self-reproachful. Admitted here 7 times from 2 to 4 months. R.

R.

(63) P. K., ♀, aged 54.

- (a) Maternal grandfather melancholy after his wife's death.

A daughter of a male cousin admitted to ment. hosp. for depress. mentis.

- (b) Sensitive, but otherwise natural, glad, even-tempered.

- (c) Leptosome, lean.

- (d) (1) At age of 25, depression of similar nature for 1 year. Since then, complete well-being.

- (2) Present depression >1 year: depressed, gloomy, self-disparaging, self-reproachful, lacking energy. Admitted to the Viborg Ment. Hosp., later here. Gloomy, stagnant, inhibited, self-disparaging, self-reproachful, often weeping.

U.

(recommended for the Viborg Ment. Hosp.)

E. J., ♂, aged 46.

- (a) Mother nervous.

- (b) Natural, even-tempered, intelligent.

- (c) Uncharacteristic (deformity of back).

- (d) (1) At age of 29, first depression, since then 4 or 5 attacks: becomes sleepless, reserved, highly self-disparaging, slight suic. ideas. Admiss. three times to the psych. department of the Frederiksberg Hosp. depress. mentis periodica. "Filadelfia" depression 10 months in all.

When admitted, gloomy, depressed, self-reproachful, self-disparaging. Rapid improvement.

R.

(65) A. C., ♀, aged 68.

(a) No predisposition.

(b)

(c) Pyknic.

(d) For the past 10 to 15 years, periodical depressions of some months' duration, with lack of energy, low spirits, not sleeping well.

I. (senile (c) Present depression > 3 months.
dementia).

THREE TYPICAL CASES OF DEPRESSIO MENTIS PERIODICA

(I) ♂ M., born on June 23rd 1889. Case record No. 21,492.

Predisposition: his mother suffered from depression, committed suicide by hanging at the age of 59 years. Two maternal aunts also suffered from depression, one of them committed suicide by drowning at the age of 60 years, the other died in a private hospital at the age of 43. His maternal grandfather was also depressed, but was never admitted to hospital; he died of old age. His father, too, took a serious outlook on life, but as far as is known, he was not very depressed.

The patient himself has always been sensitive, readily gets sorry, but otherwise, during his healthy periods, he has been in a fairly good humour.

In 1917 the patient had his first period of depression. He became restless and was in low spirits but was still able, though with difficulty, to attend to his work. This state went on for about 6 months, but the patient recovered under treatment and was feeling well until 1934, when he again became fatigued, indisposed and was in low spirits and, as he could not manage his work, was admitted for some time to the "Hald Folkekuranstalt". Since then he has had several periods of depression, among others in 1938, 43 and 45. They are often released by too much work, but generally they abate spontaneously. His longest period of depression was in 1938-39, lasting 21 months. The patient has never had any periods of exaltation.

In 1943 he was given 8 electroshocks, after which the depression was obviated. During his stay at the Dianalund Nerve Sanatorium from Sept. 24th to Dec. 3rd, 1946, the patient gave a good description of the attacks with their distinct periodicity. In particular it has struck the patient that each attack abates "as if an electrical button is pressed", after which he feels well and fit for work after being down-hearted and fatigued for months, looking at his work and preferring to rest on the divan. Under the ordinary course of treatment, with occupational therapy, the depression subsided and the patient was discharged in well-being.

Index (Strömgren) + 0.1.

(II) ♀ T.-J., born in Aug. 15th 1904. Case record No. 21,483.

Predisposition: the patient's father has been in the psychiatric department of the Frederiksberg Hospital under the diagnosis: neurasthenia gravis, melancholia. During her stay there she was depressed, anxious, attempted suicide, and was transferred to the Oringe Mental Hospital. The patient's mother is very melancholy. A brother and a sister suffer from depression and the patient's 17-year-old daughter has been in hospital twice for depression.

The patient was in completely good health until her first period of depression in April 1944, when, without any external causation whatever, she got a depression which lasted about two months. Afterwards the patient was in completely good health and in fairly good humour until Nov. 1944, when a similar condition developed and persisted till April 1945. During the third period, from July to October 1945, the patient was in the neurological department of the Frederiksberg Hospital under the diagnosis: depressio mentis, psychosis manio-depressiva? Here she was given a pentazole shock, which took her into her habitual condition. During her fourth period of depression, which began at the end of April and lasted till July 19th 1946, she was re-admitted to the Frederiksberg Hospital. She was then given two pentazole shocks which produced

a transient improvement, for which reason she had three shocks at home, with resulting recovery. She was in good health until the fifth period of depression set in in September, when she became depressed, uneasy, restless, anxious, and therefore was admitted here.

During her stay in the Nerve Sanatorium her condition was somewhat fluctuating, as she was weeping in the morning, but smiling in the evening. She had a good knowledge of her disease and realized that the condition is hereditary and recurring at intervals. Her condition improved under the ordinary course of treatment and opium therapy.

She was discharged to spend her convalescence at a country boarding house.

Index (Strömgren) — 0.9.

(III) ♀ P., born on Sept. 29th 1892. Case record No. 21,761.

Predisposition: the patient's mother was very melancholy, committed suicide by hanging at the age of 60.

During the last 15 years before her first admission to the colony the patient has been suffering during periods of depression setting in by attacks about every other year. They frequently began in spring, persisting for 5 or 6 months, during which time the patient generally had to keep her bed for 1 or 2 months. When the depression has been obviated, the patient is in completely good health and fit for work, and quite even-tempered. The patient never had any manic phases. During her periods of depression the patient is often weeping without any cause, is not, however, tired of life, is ruminating a great deal, reproaching herself, thinking she is unable to do anything, cannot get started with her work, is over-sensitive to noise, does not sleep well and therefore has to use hypnotics; is worried about how they are getting on at home.

In the course of the years the attacks have become rarer and of shorter duration; still, the shortest attack has been for 7 months, in 1945.

During her last stay, from Dec. 10th, 1946, to Febr. 1st, 1947, the patient was treated with 4 pentazole shocks after

which she recovered, became smiling and glad and was discharged 3 weeks later as recovered.

Index (Strömgren) + 0.4.

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Outline of 33 cases of
with measuring

Name	Admiss. Discharge	Diagnosis	Predisposition
69. F. C. ♂ 20/4 1913 aged 33	30/1 13/3 1946	Depr. m. period.	No predisposition for depr. in family
70. E. M. H. ♀ 30/3 1910 aged 36	16/3—2/8 1946	Depr. m. period., imperative conceptions	A maternal aunt nervous. None of her family depressed.
71. E. K. C. ♀ 14/8 1913 aged 33	6/6—30/8 1946	Depr. m. period.	None of her family depressed.
72. J. M. P. ♀ 29/9 1892 aged 54	4/2—10/3 1939 17/3—4/4 1941 2/10—6/11 1946 10/12—1/2 1947	Depr. m. period., menopause	Mother melancholy.
73. M. K. M. ♂ 23/6 1889 aged 57	24/9—3/12 1946	Depr. m. period.	Mother, 2 maternal aunts, and maternal grandfather suff. from depr. 2 suic., fa- ther grove
74. O. I. A. J. ♀ 22/1 1910 aged 37	10/9—7/12 1946	Depr. m. period. endogenous, hysteriform.	None of her family depressed.
75. H. S. K. ♂ 2/8 1896 aged 50	29/7—10/12 1946	Depr. m. period.	No predisposition
76. K. V. G. ♂ 28/6 1879 aged 67	15/10—15/12 1946	Depr. m. period. familiaris. Dementia senilis?	Mother depressed, about 50 years old in ment. hosp. A brother here: neurasthe- nia. A male cousin's daughter Dr. Gram
77. J. J. H. ♂ 16/8 1890 aged 56	6 times from 1935—1946 2/11—21/12 1946	Depr. m. period. (Hypomaniac phases)	Father somewhat melancholy. Brother nervous.

depressio mentis periodica.
of „Index“.

Number of attacks	Result of treatment	Index	Special treatment	Manic phase
3	I.	1.3		
4	I. (R)?	-- 0.9	Shock (electro)	
2	R. (?)	-- 0.3		
Many attacks since youth, about every other year	R. R. (?) R. (?) R. (?)	+ 0.4	Shock (pentazole) during last stay	
5	I.	+ 0.1		
4	I.	-- 0.9		
Numerous	R.	+ 0.2	Shock (pentazole) 4 times	
3	U.	-- 0.2		
Numerous	R.	+ 0.5	8 pentazole shocks	

TABLE

Name	Admiss. Discharge	Diagnosis	Predisposition
78. A. H. S. ♂ 19/10 1880 aged 66	15/4 46— 1/1 1947	Depr. m. period.	A sister has had a single depr., was adm. to the „Korhuset“ about 20 years ago. No other depr. in fam. Father ruminating temperament
79. A. L. ♂ 7/5 1920 aged 26	21/10 46— 11/1 1947	Depr. m. endo- gen. periodica familiaris	Mother adm. here for 3 depr. Mother's female cousin said to have had simil. case, was adm. to Middelfart Ment. Hosp.—Maternal grandmother cheerful but period. melanch. in climact. and old age. 3 suic. in mother's family
80. E. T.-J. ♀ 15/8 1904 aged 42	19/9 46 27/1 1947	Psychosis ma- nio-depressiva in constit. hysteriforme	Father adm. for neurasthenia gravis, depr. during stay, attempt. suic., transf. to Oringe Ment. Hosp.—Mother very melancholy, a brother and a sister depr.
81. M. N. ♀ 26/2 1912 aged 35	19/7 46 15/9 1946 11/11 46 15/2 1947	Depr. m. period. (endogenous?)	No known cases of depr. in family
82. V. S. ♀ 20/2 1891 aged 56	14/1—1/3 1941 3/7—5/11 1941 26/9—17/12 1942 22/1—18/3 1947	I, II, III Depr m. period. IV Psychopathia	Some nervousness in father's fam. Father himself always grove?
83. A. C. A. H. ♂ 21/9 1915 aged 31	31/1—31/3 1947	Depr. m. endo- genous period. familiaris	Father has been depr. A brother and a sister have been adm. here. Brother: d. m. p. famil. Sister: d. m. period. Case record states that sister is manic-depressive and has been adm. to Viborg Ment. Hosp.
84. A. M. B.-S. ♀ 29/10 1906 aged 40	30/12 43 2/2 1944 3/3—21/4 1947	Depr. m. period. Psychoinfan- tilismus	Father repeatedly depressed. A paternal aunt adm. many years ago for depression. Does not know much of her fam.
85. I. K. W. ♀ 19/7 1899 aged 48	22/5—26/7 1947	Melancholia periodica fam., menopause	Father melancholy
86. J. H. P. I. ♀ 25/1 1910 aged 37	18/3—31/7 1947	Psychopathia. Depr. m. period. fam.	Father's family much inclined to be „out of sorts“. A female cousin epileptic.

I

Number of attacks	Result of treatment	Index	Special treatment	Manic phase
Several short periods.	R. (?)	— 0.5		
12	R.	— 0.4	5 pentazole shocks	
5	I.	— 0.9	Pentazole shock (+ azoman)	
3	R. R.	- 0.4	Pentazole shocks and electroshock	
Numerous	R. (?)	— 0.3	Pentazole shocks 1942 and 1947	
Always melancholy 2	R.	+ 0.3	Pentazole shock 4 times	
Numerous	I.	0.0		
3	R.	— 0.3		
Numerous	I.	— 0.5	4 pentazole shocks 1946	

TABLE I

Name	Admiss. Discharge	Diagnosis	Predisposition
87. A. A. R. ♀ 15 3 1906 aged 41	18 3—2 8 1947	Depr. m. period., menopause	Maternal great grandfather melancholy. Maternal grandmother's sister also transiently depressed
88. E. T. E. A. ♀ 3/7 1907 aged 40	19 11 46— 18/1 1947 17,5—4/8 1947	Depr. m. period.	A brother somewhat retarded
89. A. C. G. ♀ 23/5 1905 aged 42	26,7—9 8 1947	Depr. m. period.	Paternal grandmother confined to bed for 17 years. A male cousin undoubtedly depressed
90. M. A. D. ♀ 4/7 1915 aged 32	12 5—12 8 1947	Depr. m. period.	Father very nervous. A female cousin has been adm. here for psychopathia. A male cousin comm. suic. at age of 16 (paternal uncle's son). Paternal grandmother somewhat gloomy
91. I. E. T. ♀ 9 8 1893 aged 54	12,4—15/8 1947	Melancholia period. anxiosa. Pel-lagra. Fract. col.	Father depressed. A sister here: depr. mentis endogen. Dem. senilis incip.
92. M. E. H. ♀ 4/1 1896 aged 51	24,5—23 8 1947	Depr. m. period. Hypertrophia cordis	A Swedish maternal aunt undoubtedly insane, may have been depression. Mother sometimes had a dark outlook of life
93. C. M. A. ♀ 10 6 1904 aged 43	7,2—11/10 1947	Melancholia period.	A sister depressed now and again
94. U. E. H. ♀ 12,10 1885 aged 62	20 6—12,9 1947	Melancholia period. Ulcus cruris sin.	Several brothers and sisters are nervous
95. M. P. S. ♂ 18 6 1910 aged 37	30 6—20 9 1947	Depr. m. period. Meningo-myelitis	Paternal grandmother's sister schizophrenic. Several relatives in ment. hosp. for schizophrenia. Paternal grandfather melancholy, suic. Paternal grandfather's brother and sister insane. Maternal aunt: paranoia, possibly schizophrenic.
96. H. V. J. ♂ 1 1 1909 aged 38	6 8—20 9 1947	Melancholia period.	Father: ps. manio-depr.

(cont.)

Number of attacks	Result of treatment	Index	Special treatment	Manic phase
4—5	I	— 1.1	4 pentazole shocks. Previously 13 electroshocks at St. Josef's Hosp., Aarhus, with transient effect. 1946	
3?	R.	— 0.5	—	
4	R.	— 1.3	—	
5—6	R. (?)	— 1.1	Shock treatment in 1939 and 1943 at Univ. Hosp. Here 7 electroshocks	
3	U.	— 1.4	6 pentazole shocks in 1947	
2	R.	+ 0.1	—	
Numerous	R. (?)	— 0.1	Several shocks	
2	I.	— 0.4	—	
4	I.	— 1.2	—	
2	R.	— 0.3	5 electroshocks in 1942. Pentazole shock in 1947	

TABLE I

Name	Admiss. Discharge	Diagnosis	Predisposition
97. J. R. T. ♂ 4 3 1920 aged 27	19 5—10 9 1947	Depr. m. period.	None
98. R. M. K. ♀ 5 12 1903 aged 43	31 7 34—14 4 36 5 10 1942 19 4 1943 6 6 1947	Depr. m. period. Alimentary hypoglycemia Menopause	Father several times in ment. hosp. for depr. 2 paternal uncles epileptics. A sister nervous
99. P. A. N. ♀ 30 7 1900 aged 47	18 6—17 9 1947	Depr. m. period. hysteriformes. Eczema cruris Ulcer cruris seq.	At age of 13 her son was in psych. department of Univ. State Hosp. (suicide in 1946)
100. A. M. A. ♀ 14 5 1897 aged 50	8 7—6 9 1947	Depr. m. period. Menopause	Mother often depressed. A brother died in Viborg Ment. Hosp.
101. E. V. W. F. C. ♀ 11 3 1919 aged 28	8 11—19 12 1944 23/3—24 5 1946 4 8—30 9 1947	Depr. m. period.	Father suffered from „nervousness“ for many years. A paternal aunt comm. suic. with gas. A male cousin of her father's schizophrenic.
102. E. A. ♀ 30 3 1905 aged 42	15 10—20 12 1945 28 8 1947	Depr. m. period.	A paternal uncle is queer

(cont.)

Number of attacks	Result of treatment	Index	Special treatment	Manic phase
Several	R.	— 0.1	6 pentazole shocks	
Numerous		— 1.2	6 electroshocks in 1943. 2 pentazole + 3 electro- shocks in 1947	
Several	I.	— 0.7	—	
5 (about every 6th year)	R.	— 0.9	3 electroshocks in March 1947 in Odense	
Numerous	R.	— 0.4	5 electroshocks	
3		— 1.0		

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ABACTERIAL MENINGO-ENCEPHALITIS WITH INCREASED PROTEIN CONTENT IN THE CEREBROSPINAL FLUID¹

BY
MOGENS TRIER,
M.D.

Since April 1945 eight patients² have been admitted to the Medical Department of the Frederiksborg Amts Centralsygehus (hereafter called the FAC) suffering from acute-subacute meningitis or meningo-encephalitis. The disease was characterised by sterility of the cerebrospinal fluid, which presented varying degrees of pleocytosis and a high content of albumin and globulin, combined with typical meningeal symptoms but without any other definite neurological signs.

To the medical staff it was remarkable to meet with so many cases of this characteristic but to us unknown facies morbi, and we feel justified in submitting our observations to the Danish Neurological Society to-day in the hope that this most competent gathering might furnish us with information of similar cases and of the more precise nature of the disease.

I shall now give an extract of the eight case records.

Patient No. 1.

Case record B 738/45. 45-year old leather worker admitted on April 25th, 1945 to the ear department of the FAC for vertigo. About four weeks before admission the patient had a sudden attack of giddiness with severe

¹ Paper read at the meeting of the Danish Neurological Society on June 10th, 1947.

² Patient No. 8 was admitted after the reading of this paper.

frontal-parietal headache and nausea, afterwards constant headaches and sickness with varying degrees of giddiness, fatigue, and drowsiness, but though he slept most of the time he had been easy to wake up. Not feverish.

Physical (incl. otological) examination on admission: nothing abnormal. *Ophthalmological examination*: nothing abnormal. *Neurological examination*: the patient was somewhat drowsy but easy to wake up. Slight rigidity of neck, left knee jerk very weak, right almost normal. Possibly a case of meningitis or meningeal irritation as a result of an unknown infection. Temperature: normal. Sedimentation rate of erythrocytes: 13 mm/1 hour. Leucocytes/mm³: 5880. Differential count normal. *Cerebrospinal fluid*: cf. Table 1.

On May 2nd the patient was transferred to the medical department for meningo-encephalitis. Here the X-ray examination revealed a pulmonary infiltration which did not subside during the patient's stay in hospital (no sputum, stomach washing 3 times: $\div$ Tb). X-ray of the skull and porus acust. int.: nothing abnormal. Wassermann reaction: negative. Weil reaction: negative.

His temperature remained normal (except during an acute attack of tonsillitis) and after two weeks in bed the patient felt perfectly well. On June 7th he was transferred to a local hospital for continued treatment of the pulmonary infiltration, which was decreasing when he left hospital on July 18th.

TABLE 1.

Patient No. 1	Cerebrospinal fluid				
Date	28/4	29/4	5/5	11/5	29/5
Pressure, mm H ₂ O	100/70			120/80	
Cells per 3 mm ³	123	148	180	232	72
Albumin } Bisgaard		40	20	22	22
Globulin } method		3	3	3	2
Glucose mg%		66		54	71
Bacteria { direct microscopy		none			
Bacteria { culture		no growth			
Wassermann reaction		negative			

Patient No. 2.

Case record B 1057/46. 67-year old widow. On July 7th, 1946, admitted to the ear department of the FAC for paresis of the left facial nerve. Has been suffering from increasing deafness with pulsating tinnitus for 3-4 years. A fortnight before admission headaches, pains at the back of

the head, rigidity of the neck, parasthesiae in arms and hands and since then severe headaches with varying degrees of giddiness. Six days before admission the patient's face suddenly became skew, she could not close her left eye nor drink out of a cup. Not feverish.

Physical (incl. otological) examination on admission revealed a left peripheral paresis of the facial nerve, sense of smell extinct in the left side of the nose, sense of taste extinct in the left front part of the tongue, and hearing reduced on both ears. *Ophthalmological examination:* angiopathia hypertonica l.g., lagophthalmus o. sin. *Neurological examination:* indistinct speech, raucous voice. Evident paresis of the left facial nerve. The patient cannot contract her forehead on either side nor actively move the region of the right facial nerve region, which might indicate a bilateral peripheral paresis of the facial nerve. Temperature: subfebrile. Sedimentation rate: 38 mm/1 hour. Blood pressure 210/100. Leucocytes/mm³: 4520. Differential count normal. Wassermann reaction negative. *Cerebrospinal fluid:* cf. Table 2.

On July 9th the patient was transferred to the medical department for rheumatic paresis of the facial nerve and observation for a cerebral tumour. At this department a hypertensive cardiac disease was also demonstrated. The patient was kept in bed, and her condition improved steadily. At first her temperature was slightly above normal (max. 37.8° C), later normal. Sedimentation rate remained above normal (50-46-34-42-45 mm). Her headaches and giddiness disappeared, her voice became normal, the facial paresis decreased, and on leaving hospital on Sept. 4th the patient was feeling well.

TABLE 2.

Patient No. 2	Cerebrospinal fluid					
	4/7	7/7	15/7	25/7	14/8	28/8
Date	4/7	7/7	15/7	25/7	14/8	28/8
Pressure, mm H ₂ O	260/140	200/100	100/70			
Cells per 3 mm ³	204	212	232	162	92	34
Type of cells.....			mononuclear			
Albumin } Bisgaard ..	28	30	22	28	26	24
Globulin } method	10	10	3	<10	4	3
Glucose mg%	75	79		50		
Wassermann reaction		neg.	neg.			

Patient No. 3.

Case record B 1400/46. 40-year old widow. In a local hospital from Oct. 23rd to Nov. 28th, 1945. Diagnosis: cerebrospinal meningitis. For some years at intervals of 1-2 weeks the patient had suffered from head-

aches localized at the back and top of the head. Before her admission to hospital her headaches grew worse. The day before she had a temperature and numerous attacks of vomiting and on the day of admission she suddenly had difficulty in swallowing. No paraesthesiae or sensory disturbances.

Physical examination on admission: No rigidity of neck or back, no focal symptoms. *Cerebrospinal fluid*: cf. Table 3. Sedimentation rate: 7 mm/1 hour. Therapy: Cibazol for five days. Temperature: subfebrile-normal.

Admitted to the medical department of the FAC for sequels of meningitis Sept. 18th, 1946. After her stay in the local hospital she had still suffered from severe headaches "like a cap of iron" for a few days at a time and occasional giddiness. She still had difficulty in swallowing, her food could not pass but had to be washed down. She felt tired and nervous.

Physical examination on admission: nothing abnormal. *Ophthalmological examination*: nothing abnormal. *Otological examination*: nothing abnormal. *Neurological examination*: neurologically nothing abnormal. Muscles of shoulders, back of head and neck very tender, presumably due to myoses not connected with the meningitis. No neurological explanation of the afore-mentioned difficulty in swallowing. Temperature: normal. Sedimentation rate: 11-10-7-8 mm/1 hour. Wassermann reaction negative. X-ray of oesophagus: normal. *Encephalography*: sparse filling of the ventricles, no dislocation of the ventricular system.

The patient's headaches were considerably improved by physiotherapy.

TABLE 3

Patient No. 3		Cerebrospinal fluid					
Date	1945	(1)	(2)	(3)	1946	1/11	12/11
Cells per 3 mm ³		77	25	3		2	6
Albumin } Bisgaard.....		80	<10			16	14
Globulin } method		6	4			>1<10	3
Bacteria { direct microscopy		none					
Bacteria { culture		no growth					
Wassermann reaction		negative					

Patient No. 4.

Case record B 1521/46. 45-year old lorry driver. Admitted to the medical department of the FAC on Nov. 4th, 1946 for observation for intracranial trouble. Since childhood the patient had suffered from migraine about once a week but had improved with time. Six days before

admission he had "influenza" with headaches, pains in the back and the limbs, and a temperature. Since then he had been feeling gradually worse, had for the preceding 24 hours suffered from unbearable headache (not like migraine), giddiness, nausea, and numerous attacks of vomiting. Pulse taken by the doctor: 46 per min.

Physical examination on admission: the patient was in pain, restless and distressed, but quite conscious and orientated with a slight rigidity of the back. *Ophthalmological examination*: nothing abnormal. *Neurological examination*: some rigidity of neck, Kernig symptom positive, otherwise nothing abnormal. Temperature: 38.4° C. Pulse: 60. Blood pressure: 150/90. Sedimentation rate: 5 mm/1 hour. Wassermann reaction: negative. X-ray of skull: nothing abnormal. *Cerebrospinal fluid*: cf. Table 4.

After five days treatment with penicillin and sulphathiazol the patient's condition quickly improved, and from the fifth day the temperature was normal. During his stay in hospital he had some attacks of migraine, but otherwise no headaches. Sedimentation rate: 8.5 mm/1 hour. Discharged on Dec. 14th feeling perfectly well.

TABLE 4

Patient No. 4	Cerebrospinal fluid						
Date	4/11	5/11	8/11	11/11	19/11	2/12	7/12
Pressure, mm H ₂ O	80/		110/	180/			
Cells per 3 mm ³	1600	1280	1584	256	272	92	47
Type of cells	mononuclear						
Albumin } Bisgaard	60	60	40	30	15		17
Globulin } method	6	4	4	3	2		1
Glucose mg%	67						
Bacteria { direct microscopy	none						
Bacteria { culture	no growth						
Wassermann reaction	negative						

Patient No. 5.

Case record B 1439/46. 37-year old storekeeper. Admitted to the otological department of the FAC for frontal sinusitis. For the last fortnight the patient had been suffering from pains at the front and back of the head, giddiness, sickness, and vomiting, for the last 24 hours also from flickering before the eyes. Not feverish.

Physical (incl. otological) examination on admission: Somnolent with slow cerebration, slight euphoria, otherwise normal. Temperature: normal. Sedimentation rate: 7 mm/1 hour. *Ophthalmological examination*: nothing abnormal. X-ray of nasal sinuses: nothing abnormal. Wassermann

reaction: negative. Leucocytes/mm³: 11200. Differential count normal. *Cerebrospinal fluid*: cf. Table 5.

On Nov. 7th transferred to the neuro-surgical department of the Rigs-hospital to be observed for intracranial trouble. X-ray of skull: nothing abnormal. Ventriculography: diffuse dilatation of the ventricular system, which has a central position, third and fourth ventricles in situ. Treated with penicillin and sulphamethylizol for five days.

On Nov. 15th transferred to the medical department of the FAC for meningo-encephalitis. During his whole stay he was restless, twaddly, and silly, had visionary and auditory hallucinations at night. The temperature was constantly normal. Sedimentation rate: 7-16 mm/1 hour.

Transferred to the psychiatric department of the Righospital on Nov. 26th. On arrival the patient was fully conscious and orientated, refused to enter hospital, and was therefore sent home. His medical adviser states that during the first week following his discharge the patient became lucid and has since been perfectly well.

TABLE 5

Patient No. 5	Cerebro-spinal fluid	Cisternal fluid	Ventri-cular fluid	Cerebro-spinal fluid
Date	6/11	8/11	12/11	19/11
Pressure, mm H ₂ O	500/100			
Cells per 3 mm ³	888	1040	211	704
Type of cells				chiefly mononuel.
Albumin } Bisgaard	60	60	50	> 90
Globulin } method	8	8-9	4	> 10
Bacteria { direct microscopy	none			none
{ culture	no growth			no growth
Wassermann reaction	negative			negative

Patient No. 6.

Case record B 285/47. 52-year old waiter. Admitted to the medical department of the FAC on Jan. 6th, 1947, for pneumonia, under observation for empyema and meningitis. Ten days before admission the patient was suddenly taken ill with cold shivers and a high temperature. Two days later he felt a stitch in the right side of the chest, he coughed and expectorated. After four days' treatment with penicillin at home the patient's temperature fell to normal. Two days before admission the temperature rose to 40° C, the patient had headaches, pains at the front and the back of the head, and was confused.

TABLE 6

Patient No. 6		Cerebrospinal fluid									
Date		6/1	8/1	11/1	17/1	23/1	6/2	13/2	4/3		
Pressure, mm H ₂ O		120/80	140/80	110/80	50/30	90/60	130/110				
Cells per 3 mm ³		12000	12400	6400	240	66	56	14	160/140		
Type of cells		polynuclear							0		
Albumin (Bisgaard)		70	80	80	50	30	28	14	15		
Globulin { method		>10	>10	>10	10	4	3	2	2		
Bacteria { direct microscopy		none	none	none	none						
Wassermann reaction { culture		no growth	no growth	no growth	no growth						
		negative	negative								

Physical examination on admission: highly febrile, exhausted, drowsy, rigidity of neck and back, but otherwise no neurological symptoms. Stethoscopical examination and X-ray revealed remains of pneumonia in the right lung. *Ophthalmological examination*: nothing abnormal. Sedimentation rate: 100 mm/1 hour. Sputum: pneumococci type 23, no TB on direct microscopy and culture (twice). *Cerebrospinal fluid*: no TB on direct microscopy and culture (twice), otherwise cf. Table 6. Leucocytes/mm³: 21800-8840-3320. Differential count: 11-3 per cent rod-shaped neutrophils, otherwise normal. Wassermann reaction: negative.

Penicillin was administered intramuscularly for 18 days and intraspinally for 10 days, as well as sulphathiazol by mouth. After four days the patient's temperature fell to normal and remained so for the rest of his stay. Sedimentation rate: 88-61-74-45 mm/1 hour. 21 lumbar-punctures were made, the cerebrospinal fluid was examined sixteen times for bacteria by direct microscopy and by culture, always with negative result. On March 17th the patient was discharged feeling perfectly well.

Patient No. 7.

Case record B 669/47. 53-year old mechanic. On April 26th, 1947, admitted to the surgical department of the FAC for concussion. Directly before admission he was found at the bottom of a well in 20 in. of water. When admitted to the hospital he was drenched and numb, shivering with cold, twaddly, and very loquacious, his speech was indistinct and his voice hoarse. He complained of pains in the left side of the neck and of giddiness. He remembered having consumed 10-12 bottles of beer (light lager) during the day, otherwise he does not remember what has happened. Apart from a small hematoma at the back of the head nothing abnormal was found. Sedimentation rate: 6 mm/1 hour. Temperature: slightly above normal for the two first days, afterwards normal. With bed rest the patient's headache and giddiness disappeared, and on the eighth day, May 3rd, he was discharged feeling perfectly well.

Three days later, on May 6th, he was admitted to the medical department of the hospital for sequel of concussion, fever, and under observation for pneumonia. On his return home a constant, throbbing, frontal and temporal headache set in which was aggravated with pressure and when he was sitting up. For the last few nights he had not slept on account of headache. The day before admission the patient started shivering with cold and his temperature rose to 41° C, the following day he felt sick and vomited once.

Physical examination on admission: Patient extremely febrile, but not distressed. Questionable rigidity of neck, otherwise nothing abnormal. *Ophthalmological examination*: conjunctivitis, otherwise normal conditions. *Neurological examination*: slight ptosis of left eyelid. Very slight indication of Babinski sign on the left side. X-ray of skull, nasal sinuses,

TABLE 7

Patient No. 7		Cerebrospinal fluid						
Date		7/5	8/5	12/5	16/5	23/5	30/5	6/6
Pressure, mm H ₂ O		150/60						
Cells per 3 mm ³		132	116	450	133	132	270	41
Type of cells		polynuclears						
Albumin } Bisgaard		30	30	40	22	20	19	16
Globulin } method		2	1	3	3	2	3	2
Glucose mg%		145	135	87	69	44	46	
Bacteria { direct microscopy		none	none	none	none	none	none	
{ culture		no growth	no growth	no growth	no growth	no growth	no growth	
Wassermann reaction		negative						

and lungs: nothing abnormal. Sedimentation rate: 25 mm/1 hour. Wassermann, Weil, and Widal reactions: negative. Blood culture (five times): no growth. Leucocytes/mm³: 14900. Differential count: 30 per cent rod-shaped neutrophils, 53 per cent segmented neutrophils, 16 per cent lymphocytes, 1 per cent monocytes. *Cerebrospinal fluid*: cf. Table 7.

The patient was treated with penicillin and sulphathiazol for one week after which he developed exanthema. His temperature fell lytically to about 38° C, but simultaneously with the outbreak of the exanthema it rose and was much higher for 48 hours whereupon it fell and remained normal. Sedimentation rate: 61-36-23-14 mm/1 hour. The patient's headaches disappeared in less than a week, and since he felt well. On June 7th he was discharged feeling completely recovered.

Patient No. 8.

Case record B 910/47. 50-year old labourer. Admitted to the medical department of the FAC on July 31th, 1947, for encephalitis and observation for cerebral tumour. Since childhood the patient's hearing had been reduced on the left ear. 2-3 weeks before admission sudden violent frontal-parietal headaches set in which became constant. The patient also suffered from giddiness, nausea, and was increasingly dazed. He was able to sleep all the time and was occasionally confused. No convulsions or pareses. Temperature normal.

Physical examination on admission: the patient was dazed, he spoke slowly and with difficulty, otherwise no certain pathological symptoms were revealed. Kernig's sign negative. *Ophthalmological examination*: nothing definitely pathological. *Neurological examination*: psychically unusual, complete lack of spontaneity, but gives intelligent and precise answers to questions. No actual aphasia, but difficulty in finding his words. Dizzy when sitting up. Walks carefully with short steps but without a definite lurch. An intracranial affection is probably present in the frontal region (tumour?). Temperature: normal. Sedimentation rate: 7 mm/1 hour. Wassermann and Weil reactions: negative. X-ray of skull: normal. *Cerebrospinal fluid*: cf. Table 8.

During his stay in hospital the patient was periodically confused, his speech was incoherent, he jumped about the room and was rather violent, but not aggressive. On Aug. 8th he was transferred to the neurosurgical department of the Rigshospital for observation. When admitted to the latter hospital he was considerably confused, but became gradually more lucid. *Neurological incl. ophthalmological examination*: normal. *Otological examination*: a chronic, suppurative otitis media of the left side. *Electroencephalography*: normal. *Suboccipital encephalography*: pressure 400, the air has preceded to the surface. *Ventriculography*: pressure 110, the picture indicated dilatation of the frontal part of both side ventricles, otherwise normal conditions. Temperature: normal. Sedimentation

TABLE 8

Patient No. 8		Cerebro-spinal fluid	Cisternal fluid		Cerebrospinal fluid			
Date	4/8	12/8	15/8	23/8	28/8	10/9	17/9	24/9
Pressure, mm H ₂ O		230/	170/50		400/			
Cells per 3 mm ³	6140	1160	656	528	260	288	128	188
Type of cells	mono-nucl.			mono-nucl.		chiefly mononuc.	mono-nucl.	mono-nucl.
Albumin } Bisgaard	50	75	58	60-65	55-60	50	40	40
Globulin } method	6	7-8	5-6	6	5-6	2	1	3
Glucose mg%	60	54				70		61
Bacteria { direct microscopy	none				no tumour	none	none	none
{ culture	no growth				cells	no growth	no growth	no growth
TB culture	no growth					no growth	no growth	
Wassermann reaction	negative							

rate: 5 mm/1 hour. Leucocytes/mm³: 10800. Chemotherapy was installed.

The patient was re-admitted to the medical department of the FAC on Sept. 2nd. Now and during the rest of his stay he felt perfectly well and did not suffer from headaches or giddiness. Psychically normal. Sedimentation rate: 15-9-7 mm/1 hour. An operation for the chronic otitis was advised, but the patient refused. On Sept. 29th he was discharged feeling perfectly well.

Although the material is somewhat heterogeneous it is characteristic that a first examination of all the patients revealed a considerable increase of the proteins in the cerebrospinal fluid (including both albumins and globulins) together with a moderate pleocytosis (77, 132, 148, 204, 888, 1600, 6140, 12000 cells per 3 mm³) in most of the patients. The proteins decreased very slowly and more slowly than the pleocytosis so that the final examination of all patients showed an increased protein-content long after all other symptoms had disappeared.

In January and February this year T. Dalsgaard-Nielsen and H. I. Schou recorded that in the departments in their charge a significant rise in the cases of pathological cerebrospinal fluids had been observed with, apparently, no corresponding increase of neurological affections which might account for pathological cerebrospinal fluid. Both authors are of opinion that they have excluded analytical errors. Dalsgaard-Nielsen associates the increase with an unobserved infection by a neurotropic virus, and Schou attributes it to a form of meningitis—possibly encephalo-myelo-meningitis, which has become more frequent in recent years.

Partly to ensure that the hyperalbuminosis of the patients in question was not due to technical errors (which is also disproved by the *facies morbi* of all the patients) and partly to decide if pathological values have frequently been found in patients of this hospital who have not otherwise presented any clinical signs of organic nervous affections, I have gone through the case records of all patients with pathological cerebrospinal fluids who were admitted to all departments of the FAC during the period April 1946-June 1947. Like Dalsgaard-

Nielsen and Schou I have regarded all cerebrospinal fluids with an albumin figure above 15 (determined according to the Bisgaard method) as pathological.

During the said fourteen months 456 cerebrospinal fluids were examined, in 145 (32 %) of which an albumin figure above 15 was found. The percentual number of pathological cerebrospinal fluids per month varied from 0 to 53 without any definite relation to the season and without any definite rise within the said period. The records also showed that in all patients with pathological cerebrospinal fluids the clinical picture agreed well with the pathological findings—a fact which was contrary to Dalsgaard-Nielsen's and Schou's observations.

After this digression I shall return to my own data. They include records of two women and six men, *all middle-aged or elderly* (37, 40, 45, 45, 50, 52, 53, and 67 years old).

The disease set in at the following seasons: One case in the first, two in the second, one in the third, and four in the last quarter of the year.

No actual *prodromal symptoms* could be found in the patients. One of them had been suffering from pneumonia for about one week and another from "influenza" for a few days before the appearance of the meningeal symptoms.

In all patients *the initial symptoms* were meningeal: violent headaches in all cases, vertigo in seven, and vomiting in five cases. Four were febrile, and four did not feel feverish. The meningeal symptoms appeared from two days to four weeks before admission and in only one patient they were accompanied by other neurological symptoms (Patient No. 2).

On admission *the physical examination* of the patients revealed: five suffered more or less from rigidity of neck or spine, four were febrile, four afebrile. Patient No. 2 suffered from a (possibly bilateral) peripheral paresis of the facial nerve, while the seven other patients had no paresis of the cranial or peripheral nerves; nor did any of these have paraesthesiae, sensory or sphincteric disturbances. In six patients the reflexes were perfectly normal, in Patient No. 1 the knee jerks

were not quite equal, and Patient No. 7 showed a slight unilateral tendency to Babinski's sign—in other words, only dubious reflex anomalies.

The cerebrospinal fluid was pathological in all cases as the patients had been selected for this reason. The cell-count varied from 77 to 12000 per 3 mm³, the albumin figure from 28 to 80, the globulin figure from 2 to 10, and there was no connection between cell-count and protein content, e.g. the highest albumin figure being combined with the lowest cell-count (Patient No. 3). In seven patients the cerebrospinal fluid was examined for bacteria by direct microscopy and culture and proved to be sterile. In the case of Patient No. 2 such an examination unfortunately was not made. The Wassermann reaction in cerebrospinal fluid (and blood) was negative in all cases.

The course of the disease was characterised by the fact that neither the subjective nor the objective physical symptoms progressed after the patient's admission to the hospital. On the contrary, the subjective symptoms improved very quickly: headaches and giddiness decreased or vanished in a few days or, at the most, a few weeks. Seven of the patients were free from subjective symptoms—the majority for several weeks—before their discharge, while one (No. 5), whose condition did not improve during his three weeks' stay in hospital, felt perfectly well one week later.

Neither did the objective symptoms progress while the patients were in hospital (cf., however, No. 5), and, in particular, no neurological symptoms appeared.

On the other hand, the findings in the cerebrospinal fluid became but slowly more normal and not one of the patients had a normal cerebrospinal fluid when discharged after 33-71 days in the department. The tables show that at that time a normal cell-count was found in two patients only (Nos. 3 and 6). In all cases there was a more or less pronounced increase of proteins as the figures for albumin or globulin or both still were above normal, and it is characteristic of all the patients that the pathological changes—particularly the increase of

proteins—in the cerebrospinal fluid decrease very slowly—contrary to all other objective and subjective symptoms.

In spite of this a *favourable prognosis* may be expected according to the general course of the disease.

The problems of the *etiology, diagnosis, and differential diagnosis* may occasion the following remarks:

Common to all eight patients are the acute or subacute meningeal initial stage, the non-bacterial meningitis or meningo-encephalitis, the characteristic pathological changes in the cerebrospinal fluid, particularly the considerable and prolonged hyperalbuminosis (in contrast to the rapid subjective improvement), the absence of other neurological symptoms and, finally, the apparently favourable prognosis.

The more or less pronounced albumino-cytological dissociation suggests the Guillain-Barré syndrome (polyradiculoneuritis) or “neuro-myelitis hyperalbuminotica” (Antoni). In that case it must be a Guillain-Barré syndrome without radicular and polyneuritic symptoms.

In literature the term Guillain-Barré syndrome is generally reserved for cases of typical polyradiculitis (radiculoneuritis). The combination of the unknown etiology, the polyradicular paresis, the dissociated hyperalbuminosis and—as pointed out by Guillain & Barré—the good prognosis is emphasized. Later investigations, however, have proved that the disease often takes a chronic (Magnussen) or fatal (Fog & Lassen) course. Several authors have delimited the syndrome otherwise, and Antoni has supposed that a specific infectious disease exists which can only be distinguished from the classic Guillain-Barré syndrome by the absence of hyperalbuminosis. In spite of this it would hardly be expedient to extend the syndrome also to include cases like the present without paresis and without other neurological symptoms but the meningeal.

As the cases presented here must be considered abacterial we must, when considering the differential diagnosis, first of all look at other forms of non-bacterial meningitis and meningo-encephalitis.

It is possible but not probable that Patient No. 6 suffered

from pneumococcal meningitis as a complication of his pneumonia, but the five negative cultures from the cerebrospinal fluid contradict this theory. In Patient No. 7 a bacterial infection following a cranial fracture or fissure not demonstrable clinically or by X-ray cannot be excluded in spite of the negative cultures. It is, however, very unlikely, particularly on account of the low cell-count, whereas the possibility of a virus infection with this point of entry is presumably greater.

We have also considered leptospirose meningitis (Lambertsen has recorded a case of very prolonged leptospirose meningitis from our department), but I see no foundation for this view; three patients were examined with the Weil reaction, which was negative.

"Sympathetic" meningitis due to extra- or intracerebral purulent processes near the meninges can in my opinion also be excluded. Patient No. 8 suffered from a chronic suppurative otitis media, but even the otologists did not suggest that this might be the cause of his frontally located meningo-encephalitis.

Hardly any of the forms belonging to the toxic-allergic group of meningitis can be brought in, neither those with avitaminotic etiology or those due to exogenous or auto-intoxications (during the above-mentioned survey of records I found some examples of albumino-cytological dissociation in patients with uremia).

The question becomes more complicated when we consider virus meningitis. I am of opinion that the pathological picture described can reasonably be dissociated from both abortive poliomyelitis and from the benign lymphocytic "idiopathic" meningitis (described in this country by Krabbe). For one thing, in virus meningitis a large increase of protein—especially globulin—in the cerebrospinal fluid is an exception. The suggestion of epidemic encephalitis in this connection would also be rather far-fetched. To our knowledge none of the patients had been exposed to infection with parotitis, morbilli, varicellae or other vira known to cause post- or para-infectious meningo-encephalitis at a suitable time in relation

to his meningitis, and none of them presented (other) symptoms of these diseases.

I shall therefore conclude by saying that in my opinion the *facies morbi* described, viz. the abacterial hyperalbuminotic meningo-encephalitis (arachnoiditis) without radiculoneuritis symptoms and of unknown etiology (virus infection?) is a nosological entity—and I should be most interested to hear your opinion of the matter.

SUMMARY

In 1945-47 eight patients with acute-subacute meningitis or meningo-encephalitis were treated at the Medical Department of the Frederiksborg Amts Centralsygehus. They presented a pathological picture characterised by:

Sterile cerebrospinal fluid with a high albumin and globulin content and varying, most often moderate, pleocytosis, pronounced meningeal and in most cases also cerebral symptoms, but otherwise no neurological symptoms, particularly no pareses or sensory or reflex disturbances.

The patients (two women and six men) were middle-aged or elderly (37-67 years).

The course of the disease was characterised by a very gradual disappearance of the pathological changes in the cerebrospinal fluid in contrast to a speedy disappearance of all other symptoms so that the spinal fluid of all patients was still pathological on their discharge 5-10 weeks after the onset of the disease.

The etiology, diagnosis, and differential diagnosis of the disease (particularly in connection with the Guillain-Barré syndrome, is discussed.

The abacterial "hyperalbuminotic meningo-encephalitis" without radiculoneuritic symptoms described in the present work is interpreted as a specific disease, presumably a virus infection.

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AN EXAMINATION OF THE ACCURACY OF
IZIKOWITZ'S METHOD FOR THE
DETERMINATION OF TOTAL PROTEIN
AND GLOBULIN IN THE CEREBROSPINAL
FLUID

BY

CARSTEN TROLLE

After it had been shown in 1941 by *Izikowitz* that many of the methods previously employed in the determination of total protein and its fractions in the spinal fluid give unsatisfactory results, it would have been natural to abandon these methods. However, when this has not been done it must be seen, *inter alia*, on the background that the correctness of *Izikowitz's* results with his own methods has been viewed with a certain scepticism, since with his fairly complicated methodics he obtains an even very great accuracy.

However, as the question of the protein content in the cerebrospinal fluid is of some importance, I have thought it of interest to examine how exactly *Izikowitz's* methods could be made to work, in order thus to be able both to establish the importance of the fact that he has introduced exact chemical methods in the determinations of protein in the cerebrospinal fluid and to find the limitation of these methods.

I have made examinations of the total protein method and the globulin method, and my thanks are due to Dr. *Eeg-Olofsson*, who was kind enough to lend me the necessary apparatus, which he is constantly using. As I have closely followed the directions given by *Izikowitz* (1941 and 1943), I shall be

content with giving a brief description of the methods in order to give an impression of their manifold manipulations.

Total protein is precipitated at 56° C. after admixture of trichloroacetic acid so that the concentration of the latter is 9.4 per cent., after which centrifugation is made. After the precipitant has been drawn off, the centrifugate is stirred up with another portion of trichloroacetic acid and centrifuged again, and this procedure is repeated once more. After removal of nonprotein nitrogen in this manner, the centrifugate is submitted to combustion for 10 hours at 290° C. in a special oven and, after admixture of hydrogen peroxide, an additional combustion is made for 3 hours at 310° C. Precipitation, centrifugation, and combustion take place in the same cylindrical pyrex tubes with conical bottoms. These fairly large tubes require a special centrifuge. After the combustion the proportion of nitrogen is determined iodometrically according to *Teorell's* micromethod (1928) with a slight modification.

The *globulins* are precipitated with a semisaturated solution of ammonium sulphate at 56° C. After centrifugation the precipitate is stirred up once more with a semisaturated solution of ammonium sulphate, and renewed centrifugation is performed. The centrifuged precipitate is then washed with trichloroacetic acid in the manner used in the determination of total protein; the thorough washing serves to remove all traces of ammonium sulphate which, of course, would compromise the results completely. The samples are then dealt with in the same manner as the total protein samples.

In Table 1, which shows an extract of my results, I have stated the titration figures for total protein and globulin. The reason why not all results are given is that, for the sake of the statistical computation, I have left out about 20 results in which the titration figures were much higher than in the other results. In all the experiments recorded here 2 cc. of cerebrospinal fluid was used for the total protein determinations, and 8 cc. for the globulin determinations. The thiosulphate used for the titration was 1/250 normal.

According to *Izikowitz* the following formula is used for the computation of the protein quantities: protein nitrogen = $k \times \frac{B - C}{T \times n}$, where n = cerebrospinal fluid in cc., k = a constant = 291.88, and B , C and T = the quantity of thiosulphate in cc. used up respectively in blank test, test (titration

TABLE 1

Titration figures in analysis of the protein content of cerebrospinal fluid.

All total protein determinations made with 2 cc. of cerebrospinal fluid.

All globulin determinations made with 8 cc. of cerebrospinal fluid.

No.	Total Protein				Globulin			
	I	II	III	IV	I	II	III	IV
1	15.25	15.40	15.25	15.33	16.46	16.50	16.78	16.85
2	18.17	17.92	17.75	17.95	18.46	18.35	18.44	—
3	18.17	19.55	17.72	17.42	18.91	19.44	19.44	—
4	17.92	18.13	18.20	18.30	18.75	18.66	18.70	—
5	18.67	19.18	19.30	19.05	19.91	19.75	19.75	19.23
6	15.25	15.85	—	—	14.63	14.95	—	—
7	17.75	17.86	—	—	17.32	16.45	—	—
8	17.80	17.80	17.77	—	17.85	17.66	17.83	—
9	14.25	14.71	14.80	14.90	14.55	14.26	14.60	14.43
10	16.80	16.40	16.60	16.82	16.41	16.56	16.45	17.30
11	20.00	19.91	19.62	—	19.70	17.38	17.28	—
12	16.31	16.02	16.75	16.66	16.74	17.02	16.71	—
13	15.74	16.66	16.42	16.65	14.85	16.15	15.78	16.21
14	17.75	17.35	17.60	—	17.72	17.05	17.23	17.60
15	17.50	17.41	17.13	—	16.92	17.48	—	—
16	16.33	16.50	16.33	16.30	16.44	16.18	17.16	16.44
17	18.62	18.52	19.01	—	19.16	19.22	19.90	19.70
18	16.96	17.34	17.35	17.31	17.70	18.00	17.40	17.65
19	17.10	17.06	17.19	—	16.96	17.41	17.01	17.01
20	19.17	18.67	18.75	—	18.02	17.72	17.96	18.10
21	11.60	11.68	11.70	—	12.80	12.80	12.78	—
22	16.07	16.05	16.20	—	16.40	16.37	16.10	—
23	14.17	14.32	—	—	16.28	16.08	15.75	—
24	16.00	16.08	16.60	—	17.51	16.05	16.55	—
25	—	—	—	—	5.10	5.80	—	—
26	16.50	16.56	—	—	16.62	16.48	16.57	—
27	17.74	18.10	17.56	—	18.25	18.03	18.15	—
28	16.19	15.99	16.20	—	16.91	16.06	16.45	—
29	17.65	17.74	17.68	—	18.95	18.75	18.75	—
30	14.38	14.30	14.45	—	14.06	14.06	14.10	—
31	12.62	12.72	—	—	13.65	13.40	—	—
32	14.27	15.19	15.10	—	15.45	15.14	15.46	—
33	13.44	13.24	13.10	—	14.78	14.58	14.90	—
34	14.78	14.57	15.00	—	15.80	15.65	15.34	—
35	14.15	14.72	14.62	—	15.23	15.50	15.23	—
36	15.10	14.87	14.82	—	14.65	14.88	14.61	—

TABLE 1 (cont.)

No.	Total Protein				Globulin			
	I	II	III	IV	I	II	III	IV
37	13.34	13.60	13.47	—	14.60	14.89	14.68	—
38	13.62	13.18	—	—	14.96	14.44	—	—
39	13.74	14.62	14.69	—	14.70	14.68	—	—
40	14.68	15.18	15.08	—	15.20	15.46	15.48	—
41	19.80	20.00	20.01	—	20.68	20.69	20.78	—
42	18.34	14.05	18.75	—	4.30	4.14	4.07	—
43	19.64	19.61	19.48	—	20.72	20.62	20.66	—
44	21.12	21.15	21.06	—	20.80	21.07	21.42	—
45	17.76	17.86	17.70	—	17.94	17.74	17.90	—
46	19.45	19.48	19.92	—	21.13	20.08	20.03	—
47	19.16	19.17	18.86	—	20.54	21.10	20.64	—
48	19.91	19.64	—	—	20.48	19.94	—	—
49	18.24	18.34	—	—	19.18	19.60	18.98	—
50	17.36	17.70	17.56	—	—	—	—	—
51	21.14	21.27	21.24	—	21.96	21.30	21.90	—
52	20.30	20.24	—	—	19.92	19.98	—	—
53	20.64	20.63	20.75	—	21.62	21.28	21.45	—
54	16.50	16.62	—	—	21.12	20.82	—	—
55	17.54	17.69	—	—	20.63	20.00	—	—
56	19.58	19.44	—	—	—	—	—	—
57	20.42	20.69	—	—	20.70	22.82	—	—
58	22.46	22.49	—	—	22.84	22.76	—	—
59	19.20	19.20	—	—	20.86	20.52	—	—
60	22.12	22.40	—	—	23.03	23.04	—	—
61	17.50	17.64	—	—	—	—	—	—
62	21.82	21.56	—	—	22.14	22.50	—	—
63	20.72	21.30	—	—	19.25	20.90	—	—
64	20.60	20.24	—	—	21.60	21.80	—	—
65	21.98	21.90	—	—	20.90	21.40	—	—
66	22.72	22.50	—	—	23.00	22.94	—	—

figures in the table), and for standardization against 10 cc. of 0.01 n KJO_3 .

The statistical computation was made by the *I/S Statistika*. According to *Rasch's* (1941) method, they have computed the standard deviation of the individual titration results, and only then the standard deviation of the result. The standard deviation in measuring off the cerebrospinal fluid will be so slight

as compared to that of the titration results that it has not been considered in the statistical computation.

We have supposed that the individual determinations are normally distributed with a standard deviation somewhere about a mean which is insignificant in this connection, and where the standard deviation is considered independent of the level.

An estimate of the standard deviation is obtained by means of the formula:

$$s^2 = \frac{SK_1 + SK_2 + \dots}{f_1 + f_2 + \dots} = \frac{SK}{f},$$

where s is the estimated standard deviation, $SK_1, SK_2, \dots$ the sum of the squared deviations in the individual determinations, and $f_1, f_2, \dots$ the number of titrations less 1 in the individual experiments.

In order to estimate whether this s^2 may be a measure of the square of standard deviation in all the determinations and, secondly, to examine whether systematical errors occur, we employ—according to Rasch—a so-called “false χ^2 ”, taking the quantity

$$\frac{SK_i}{s^2}$$

to be distributed as χ^2 with f_i degrees of freedom. $SK_i = \sum (x_{ij} - x_i)^2$, where x_{ij} is the results belonging to the i 'th determination, $x_{i1}, x_{i2}, \dots$, and x_i is the mean of these results. We can then from a χ^2 -table find the probability of the occurrence of such a χ^2 and when this has been done for all χ^2 , it can be seen whether the distribution that has resulted may have been a chance distribution with a probability exceeding 5 per cent., which is the traditional limit.

This was done for the 4 results of measuring that are sought, total protein, globulin, blank, and T.

For the determinations of total protein we arrive at the following *hypothesis I*:

$\sum SK = 22.0865$ $f = 118$ $s^2 = 0.187$. Number of observations 65. χ^2 for No. 42 will then be found to be $= 72.4$, whilst

the correlated χ^2 -value corresponding to 2 degrees of freedom and 0.1 per cent. probability is 13.8. This value can be immediately excluded as a "gross error".

Hypothesis II is then computed from the remaining $\Sigma SK = 8.5323$ $f = 116$ $MK = 0.0736$. Number of observations 64. No. 3 will then give a $\chi^2 = 36.2$, whilst the 0.1 per cent. limit for 3 degrees of freedom is 16.3, also quite an absurd value. This value is excluded and we proceed to

Hypothesis III.

$\Sigma SK = 5.8710$ $f = 113$ $MK = 0.0520$. Number of observations 63. Two values, No. 32 and No. 39, will be seen to be at 1 per cent. Over the 70 per cent. limit there are 25 in contrast with the expected 18.9. The mean error is 3.64, which gives a $t = 1.68$. This distribution is not characterized as unreasonable at the first glance and, as the point is to find out how precisely the methods work, and as it cannot be seen how such an error can be eliminated, it is to be preferred to adhere to hypothesis III, which gives a cautious estimate of the mean error, namely

$$s - \text{mean error} = 0.228.$$

In the globulin determinations we find according to *hypothesis I*:

$\Sigma SK = 16.9366$ $f = 117$ $MK = 0.145$. Number of observations 63; this gives 3 values exceeding the 1 per cent. limit, namely Nos. 11, 57 and 63. Further, it will be seen that over 70 per cent. we have 43 values in contrast with the expected 18.9; mean error 3.6. We then reject these three values as "gross errors".

With *hypothesis II* we find:

$\Sigma SK = 9.5785$ $f = 113$ $MK = 0.00848$. Number of observations 60. In Nos. 13 and 24 we then find $\chi^2 = 14.0$ and 13.0, respectively, corresponding to the probability being between 1 and 0.1 per cent.; over 70 per cent. we have 28 values in contrast with the expected 18 with a mean error of 3.55. Therefore we cannot expect to render the χ^2 -values likely. We leave out No. 24 and find a

$\Sigma SK = 8.4773$ $f = 111$ $MK = 0.0764$. Number of observa-

tions 59. In No. 13 we then find $\chi^2 = 15.5$; below 70 per cent. we have 24 cases in contrast with the expected 17.7 with a mean error of 3.52, $1 = 1.79$. This is doubtless no quite unreasonable figure; but the χ^2 arrived at in No. 13, however, is an exceptional result which is said to occur only once in a thousand.

We leave out No. 13 and arrive at *hypothesis III.*:

$\Sigma SK = 7.2948$ $f = 108$ $MK = 0.0675$. Number of observations 58. In No. 46 we then find a $\chi^2 = 11.43$ with 2 degrees of freedom corresponding to 0.1 to 1 per cent., and over 70 per cent. we have 21 in contrast with the expected 17.1 with a mean error of 3.5. The hypothesis in question cannot be immediately invalidated. Thus we find a mean error for the globulin determinations of

$$s = \text{mean error} = 0.260.$$

Even after elimination of "gross errors" the distribution for total protein and globulin is not satisfactory, as there still seem to be too many great deviations.

The results for blanks and T have been gone through in the same manner as for total protein and globulin. *For the blank values the mean error was found to be 0.114* and the distribution was fairly good, whilst *the mean error for T is 0.026* and the distribution is good.

It should be borne in mind that the object of the examination was to find a useful measure of the standard deviation in the experiments and a method of eliminating "gross errors". Therefore it is risky if we happen to underestimate the errors. It was therefore preferred to adhere to values of deviation which may possibly be too high.

It was assumed that, theoretically, the occurrence of "gross errors" must be expected in the determinations and that they need not necessarily be so great that they could not occur also by chance deviations. Consequently, a course such as the one actually occurring must be expected. Therefore, two things should be noted.

One should be very cautious not to compare the accuracy

of determinations of two series of experiments even when "gross errors" have been eliminated.

In reality it must be admitted that the condition "the results of determinations are normally distributed" turned out to be so that it is actually inadmissible to use the method described. However, there is hardly any other way out.

An estimate of the standard deviation has now been computed for the individual quantities, and now only the computation of the standard deviation of the final result of the determinations remains.

In the case of total protein we find a standard deviation of

$$s = 1.49, \text{ or about } 7.5 \text{ per cent. of a mean of } 20,$$

whereas, for instance, if 4 determinations had been made throughout, we would find a standard deviation of 0.75, or about 3.7 per cent.

In the case of the globulin determinations we find a standard deviation of

$$s = 0.414, \text{ or about } 8.3 \text{ per cent. of a mean of } 5.$$

With 4 determinations throughout we should find

$$s = 0.207, \text{ or about } 4.1 \text{ per cent.}$$

The standard deviation in the case of the T's is insignificant for the calculation. The square of standard deviation on the results of determination proper is quite predominant and about 5 times greater than the standard deviation of the blank values, but it should be noted that if only the standard deviation of the final results is dealt with, that of the blanks will not be included.

When the accuracy obtained by me is compared to the results arrived at by *Izikowitz* and *Eeg-Olofsson*, *Nihlén* and *Brohult*, the following figures result:

TABLE 2

	Total protein		Globulin	
	Mean error f. single determ.	Mean error in % of va- lues found	Mean error f. single determ.	Mean error in % of va- lues found
Izikowitz, 1941	0.17 mg%	0.35 %	0.08 mg%	0.37 %
Izikowitz, 1943		< 1 %		< 1 %
Eeg-Olofsson, Nihlén and Brohult, 1948	1.38 mg%	2.87 %	0.39 mg%	4.48 %
		about		about
Author's results	1.49 mg%	7.5 %	0.41 mg%	8.3 %

It will be seen that there is good conformity between the mean errors found by *Eeg-Olofsson*, *Nihlén* and *Brohult* and those arrived at by me. In percentage of the values found there is, however, a fairly considerable difference, but this is due to the fact that in order to get a uniform material for the statistical treatment of the figures I selected the lowest figures (of which I had most), whereas *Eeg-Olofsson*, *Nihlén*, and *Brohult* have computed the percentage variation on the basis of the mean of their results.

As far as I can see, both *Izikowitz* and *Eeg-Olofsson*, *Nihlén* and *Brohult* compute the mean error from the results as they appear in mg%. As mentioned above, this is risky, as the distribution after the computation may be wrong.

CONCLUSION

After this examination of the accuracy of *Izikowitz's* methods I must conclude that the accuracy obtained by *Izikowitz* cannot be reproduced. I believe we have performed the determinations as exactly as possible, and I do not think that practice even for a much longer time could have rendered our examinations materially safer with a method requiring so many manipulations. The fact that *Izikowitz* has considered his own methods to be more exact than I find them to be will not, however, change the value of his very thorough criticism of previous methods. Even with the accuracy found by *Eeg-*

Olofsson, Nihlén, and Brohult, and with the one found by me, *Izikowitz's* methods mean a great advance, and they make it possible to estimate and then to discard previous, imperfect methods. By means of examinations with *Izikowitz's* methods, *Eeg-Olofsson* (1947 and 1948) and *Trolle* (1948) have been able fully to confirm *Izikowitz's* criticism of the earlier methods, which they have taken up for renewed examination.

In estimating the globulin/albumin quotient it is, however, of essential importance to know the accuracy of the *Izikowitz* methods. With the accuracy found by me the computations of this quotient become of no great value, at any rate when the protein figures of the cerebrospinal fluid are low. A few examples will illustrate this. Table 3 shows globulin/albumin quotients, whilst I have allowed the proportions of globulin and total protein to vary within a limit of twice the standard deviation.

It will be seen that the quotient varies very much and that it can be difficult to decide whether there are pathologically low quotients.

SUMMARY

The standard deviation in *Izikowitz's* methods for the determination of total protein and globulin is found to be considerably greater than stated by *Izikowitz*. I found respectively 1.49 and 0.41 mg% as compared with 0.17 and 0.08 mg% found by *Izikowitz*.

Although the *Izikowitz* methods work less accurately than supposed by him, they retain their great value in examinations of the protein content of the cerebrospinal fluid, but the computations of the globulin/albumin quotients become illusory, at any rate when the protein content is low.

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ON THE DIFFERENTIATION OF
SOME TYPICAL FORMS OF HYPNAGOGIC
HALLUCINATIONS

BY

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The purpose of this work is to define the limits of some typical manifestations of the visual hypnagogic hallucinations and to characterize them as phenomena of different nature. The knowledge of various non-pathological manifestations of hypnagogic visions is not only of a theoretical interest, but may also be of clinical importance, especially if the question has to be decided, whether or not any pathognostic significance is to be ascribed to some visual hallucinatory phenomenon.

I. DEFINITION OF CONCEPTS

The term of hypnagogic hallucination was created by Maury in 1848. Other terms proposed for the subject are, for instance, "presomnal or anthypnic sensations" (Weygandt), "hypnagogic phantasms" (Trömmner), and "les visions du demi-sommeil" (Leroy).

As to the concept itself, there are likewise divergent opinions to be dealt with, emerging from difficulties of definition, especially from the desirability of clearly separating them from dreams. In this respect two entirely different points of view have asserted themselves: *firstly*, the internal point of view, adopted by Burdach and Leroy, according to which an analysis of the phenomenon itself should make it clear whether we have to do with a hypnagogic vision or a dream image, and, *secondly*, the external point of view, advocated by Weygandt

and Schultz, and accepted also by Jaspers, who consider the subject's state of consciousness to be decisive. Thus, in the words of Jaspers, such phenomena are usually designated as hypnagogic hallucinations or hypnagogic visions (H. V.), "which appear in the period before falling asleep, from full wakefulness with closed eyes until the beginning of dreams." The two points will now be discussed somewhat further.

Leroy postulated that certain differences of contents, emphasized by him on characterizing H. V. and dreams, suffice for the differentiation between these phenomena. Leroy alleges that the H. V. are images without the character of reality, or of a creation of the imagination, or of reminiscences, and to which, in spite of their exactitude, there clings something artificial and phantastic; they never quite resemble the thing they represent. The important point, according to Leroy, is the mental attitude of the subject towards these phenomena: the H. V. do not prompt the observer to actions as do the "real" hallucinations, nor do they provoke any resolve towards activity, as do certain representations. Also the wish to be active is lacking, as well as the illusion of action, as in dreams. According to Leroy we must compare the subject having H. V. to an indifferent spectator at a play, in the case of dreaming, however, to an active participator in this play: *"le rêve est essentiellement une aventure, à laquelle le sujet croit prendre part ; les visions dont nous parlerons ici ne sont que des spectacles auxquels il assiste et à l'évolution desquels sa personnalité ne lui paraît pas directement intéressée."*

Against this assertion Schultz makes the justified objection that Leroy's criterion does not cover those forms of H. V., "which fully imitate the dream-mechanism, and which are traceable without effort to nearly everybody." Schultz on his part has proposed the following definition of the concept: "hypnagogic hallucinations are such, for the most part optical phenomena, as appear before falling asleep, and where a more or less perfect control of another sense organ (e.g. the ear) must serve as a proof of the still continuing state of wakefulness."—According to our experience Schultz's criterion, how-

ever, has some drawbacks, in the first instance because the continual perception of an accompanying noise interferes with the observation of the H. V., which is especially the case when one wants to perceive a hypnagogic audition. The second drawback consists in the possibility that the undesirable dream-phenomena will be able to obtrude themselves in fits of absence of short duration, as, for instance, can be experienced during a railway-journey, when one is dreaming and yet may have permanent acoustic perceptions (the shaking of the carriage). Thus, the employment of Schultz's criterion, will not sufficiently ensure us against the error of mistaking dreams for H. V.

In order to exclude dream phenomena it would be safer to apply *Weygandt's criterion, according to which the border between the hypnagogic state and the dream is marked by the moment when the consciousness of situation disappears.*

For a further precision of this criterion I found it useful to add the following two stipulations to Weygandt's criterion, which proved essential when carrying out observations: firstly, *the subject must be able in the hypnagogic state to retain continually the consciousness of situation* and, secondly, *the ability to carry out voluntary movements must be kept intact continuously.*

Although the state of transition from wakefulness to sleep greatly varies as to duration and characteristics in individual cases, everyone, closely observing himself in the process of falling asleep, will be able to distinguish two stages: (1) the stage of *increasing fatigue*, which may be characterized by the quantitative reduction of the conscious psychic processes; (2) the proper *hypnagogic state* or hypnagogium, the beginning of which is characterized by qualitative changes in the conscious psychic processes. The hypnagogic state—in the strict sense of the term here employed—usually does not end in sleep, but in a transition to an intermediate state, which may be characterized as a vacillation between wakefulness and

sleep, its chief distinctive mark being the interruption of the continuity of the state of consciousness by constantly intruding dream-absences. This labile intermediate state ends with the transition into dream-consciousness, which appears simultaneously with the moment of definitely falling asleep and is marked by the moment of the entire disappearance of the consciousness of situation (Fig. 1).

Continuity of the consciousness of situation:	Levels of consciousness:	Corresponding mental contents:
Intact	Wakefulness	Conscious psychic processes
	Beginning fatigue (quantitative change in the psychic processes)	Progressive narrowing of the field of consciousness
	Hypnagogic state (qualitative change in the psychic processes)	"Pure" hypnagogic hallucinations
Interrupted by dream-absences	Intermediate state (vacillation between wakefulness and sleep)	Hypnagogic hallucinations confused with dreams
Disappeared	Dream-consciousness	Dreams

Fig. 1.

Synoptic table of the changes of consciousness in the process of falling asleep and of the mental contents depending thereon.

The hypnagogic state in the sense used here is a state of consciousness utterly different from the dream-consciousness. It possesses—although usually in a slight degree only—all the essential objective marks of the wakeful states, permanent orientation and the continually present ability to notice things, to criticize the observed phenomena, and to make voluntary movements at any time. *According to our definition, the hypnagogic state is also such a state of consciousness as commences (when the feeling of fatigue begins to manifest itself or is already present) with the appearance of qualitative changes in the conscious psychic processes, and ends with the*

moment when the continuity of the consciousness of situation disappears. Therefore, the term "hypnagogic hallucination" will be applied here to such hallucinatory phenomena, manifesting themselves in different modalities of senses (visions, auditions, etc.) which are perceived within the limits of the hypnagogic state.

II. MATERIAL AND TECHNIQUE

Material.—The H.V. recorded here are a result of self-observations of three persons (physicians, aged 23-38, healthy, no eidetic disposition in the sense of Jaensch, no pathological hereditary factors traceable). The observations have been made during a period of 2 years (in one case 12 years). The material as a whole consists of 170 H.V. Moreover, the experiences drawn from a voluminous material destroyed during the war underlie the text without being used concretely.

Observation Technique.—The time of observation was nearly without exception in the evening. The observations have been carried out in dark rooms, lying down, with eyes closed. Before beginning systematical observations, the observer has to make himself familiar by experience with his own hypnagogic state and its limits, he must also be able in the hypnagogic state to retain the continuity of the consciousness of situation and to interrupt the observation voluntarily at any moment. During the appearance of the H.V. it is the task of the observer to determine, if possible, in which space the phenomenon manifests itself (external or internal imaginary space,—*äussere resp. innere Eigenraum*—used in the sense of C. Schneider), whether the contents of the H.V. can be influenced "at will", and whether these contents are connected with the observer's earlier psychic experiences, or possess a life of their own. The observer must also test whether the H.V. are dependent upon his keeping the eyes open or moving them. After the disappearance of the H.V. all that has taken place has to be firmly engraved in the observer's memory in all its details and afterwards put down in writing. In order to be able to follow up the possible somatic and psychic connections between H.V. and observer, the latter has to take into consideration his own mental contents, circumstances of life, as well as his own somatic sensations and other conditions. The description of the H.V. as well as its analysis is always carried out immediately after its appearance.

Criticism and Revision of the Material.—It seems reasonable that each observer is alone able to record and arrange his H.V. with regard to their differentiation from each other, but the necessary stipulation is that he has got the experience required. This is a question of his own judgement,

and there can be no doubt that even the most experienced self-observer can make occasional mistakes; but the possibility of such mistakes would certainly increase considerably if we tried to differentiate among the results from observations of others or from the cases reported in the literature. Thus the observer himself is the only person who is able properly to decide whether, for instance, this or that vision is connected with his previous mental contents or with certain somatic stimulations, whether it has a character of *déjà vu* or *jamais vu*, and whether he is dealing with an indifferent or an emotionally-coloured H.V., etc.

Against such an individual system of classification (i.e. such a system of differentiation among H.V. as is based upon the material collected by one observer only) the objection might of course be raised that it is encumbered with personal peculiarities, that factors unnoticed by us have been exercising their influence, and that the differentiation may be based upon accidental impressions and influences. In order to eliminate as far as possible such accidental influences we have invariably followed a certain methodological principle, namely that each observer on the strength of the results of a given observation period establishes his own preliminary system of classification. Thus, for instance, the observer during some hours registers as many visions as possible, differentiates them, and makes out a "system of classification of the state in question" which is valid only for the given period of observation. The difference in the nature of the H.V. is then traced back to the changes in certain factors (i.e. level of the hypnagogic state, influence of actual psychic and somatic stimulations at the time in question). The comparative study of several classification systems for different observation periods, collected during a considerable length of time, yields an individual classification system of the H.V. that is valid for the individual in question. If such individual classification systems are obtained from several investigators, it would be possible by means of a comparative study to eliminate the personal and accidental components and to emphasize the elements of general validity. Therefore, in contrast to a principle of investigation according to which several observers are taken as a starting point, whereas only a relatively small material from each observer is differentiated, we have employed the reverse procedure: a small number of observers collect as large a material as possible, each independently, but following the same method, differentiate it according to their own points of view and experiences, creating their own individual classification system. The comparative study of such systems, we think, will then give us a classification system of general validity.

On the Differentiation between H.V. and Dream Phenomena.—As the definition of the concept H.V. here depends upon the concept "hypnagogic state", and the latter again on the determination of its limits, it is easy to realize the importance of the most exact discrimination possible be-

tween the hypnagogic state and the state of dreaming, when practical research is being carried out and "pure" H.V. are desired.

It is evident that on trying to decide whether a certain phenomena is to be regarded as a H.V. or a dream, we always have to take into consideration the state of consciousness at the time. This methodological rule has not always been adhered to in literature, and not infrequently we meet with case reports in which phenomena which are evidently dreams, are published under the heading of hypnagogic hallucinations (e.g. Silberer and Stekel). If the suggestion made by Weygandt, according to which the moment of falling asleep is psychologically marked by the disappearance of the consciousness of situation is taken into consideration, and if it is tried to define this criterion in a more precise manner, as said above (with regard to the continuity of consciousness of situation and to the control over one's voluntary movements), a somewhat subjective, but still practically adaptable, measure may be obtained that will enable the self-observer to differentiate the hypnagogic state from the state of dreaming, and thereby hypnagogic hallucinations from dreams.

III. ATTEMPTS AT DIFFERENTIATION CASUISTIC REPORTS

Jaspers discriminates between two groups of H. V. of a different nature: (1) those appearing in the objective or external space—*leibhaftige sinnliche Erscheinungen* (Hagen), and (2) those appearing in the subjective or internal space—*eigentliche Pseudohalluzinationen* (Kandinsky). It has been pointed out by Schneider that the sole criterion of the space of appearance is in itself insufficient for determination of the substance of some visual hallucinatory phenomena. Moreover, as Schneider says, the exact determination of the space of appearance of H. V. is often connected with considerable difficulties. Probably it is owing to this circumstance that the question of external or inner space has been disregarded almost completely in the casuistry published up to now.

Schultz, on the basis of material collected by 50 observers (partly pathological cases), has divided the observers into two groups: (1) *optisch Halluzinierende*, and (2) *quasi optisch Halluzinierende*. According to Paneth, this bipartition yields but meagre results, especially because the first group, as was

to be expected, consists throughout of eidetics and visionaries. With regard to contents of the H. V., Schultz has circumscribed a group, the contents of which may be traced back to the earlier psychic experiences of the observer, and considers it as being "equivalent to dreams".

Leroy, on the basis of statements made by 4 observers and of literary casuistry, considers the H. V. as phenomena of a more or less uniform nature which have been characterized as "phantastic" appearances without any particularly noticeable connection with the subject. Leroy incidentally discriminates between two categories of H. V. appearing impromptu: (1) *les visions qui reproduisent des spectacles récemment vus*, and (2) *les visions terrifiantes stéréotypées des enfants*. As to the latter group, however, the question suggests itself whether it may not consist merely of eidetic images, as similar appearances have been described by Jaensch as *terrifying eidetic images* to which children are subject at night.

Leonhard, as a result of self-observation, describes two kinds of H. V.: (1) *deutliche, wirklichkeitsnahe Halbschlafsbilder*, and (2) *schattenhafte Einschlafsbilder*. This attempt at differentiation, however, does not seem sufficiently substantiated, as it is based upon the degree of distinctness of the H. V., which evidently depends upon the somatic state at the given time. If the somatic state of the observer in half-sleep in the morning differs from the somatic state in the evening, and the degree of distinctness of H. V. varies accordingly, this does not seem a sufficient indication for subdividing the V. H.

Hypnagogic Visions Considered from the Viewpoint of Connection with the Subject's Personality.

In contrast to those authors who are inclined to make use of such H. V. as can be characterised as "phantastic" phenomena without any especially established connection with the subject (Baillarger, Trömner, Leroy, and others), only those H. V. have been selected to form the basis of this work whose characteristic features are connected with the subject, i.e.

traceable to the personality of the observer. This connection can be contemplated either from the somatic (physiologically explainable) or the psychic (psychologically comprehensible) point of view. The former category, "visions of somatic connections", will be dealt with here, namely: visions which may be regarded as hypnagogic forms of manifestation of so-called recurrent sensations and synesthesia, the criterion being the possibility to trace the vision back to a definite somatic stimulus. The second category—"visions of psychic connections"—implies an inner connection: in a psychologically comprehensible manner the contents of these visions can be traced back to a definite psychic experience.

The fact that the appearance of the H. V. in the first case is connected with previous somatic factors, and in the second with psychic factors, cannot be interpreted as a causal genetic connection in *sensu strictu* (although phenomenologically it may suggest the existence of a causal connection), and therefore we cannot here speak of a "somatogenesis" or "psycho-genesis" in the usual meaning of the words. The appearance of a H. V. never shows a fixed temporal regularity (in the sense of physiological after-images), it depends upon the constellation of the subject at the time in question, i.e. a coincidence of several psychic and somatic factors which usually remain unknown to the observer.

VISIONS OF SOMATIC CONNECTIONS

A Visions of Memory-images.—When characterizing the substance of H. V. of somatic connections it seems useful to take as a starting point the so-called recurrent sensations. It is known that after a busy day such objects as have been intensively contemplated during it (e.g. bacteria after a strenuous microscopic examination, float and waves seen by anglers) may afterwards reappear in the shape of vivid images. These recurrent sensations, when appearing in the hypnagogic state, are regarded here as hypnagogic phenomena, as *visions of memory-images*, and they show in a most pronounced way

the characteristic features of the H. V. of somatic connections, i.e. the physiologically "explainable" appearance and the lack of psychologically comprehensible contents. The H. V. of memory-images differ from the recurrent sensations not only by a reduction in exactitude and intensity of the image, but also by the observer's altered state of consciousness. As already pointed out, the phenomenon of recurrent sensations at the moment of falling asleep is distinctly different from the same phenomenon in the wakeful state as to its comprehension, its mode of appearance and shaping; thus the concept of recurrent sensation is only a generic notion, containing as species the recurrent sensation in the wakeful state and at the period of falling asleep (Schneider).

Leroy has described similar phenomena (*les visions qui reproduisent les spectacles récemment vus*), and he also maintains that these visions never exactly correspond to the original. It is not so much the inexactness of the reproduction as the possibility of tracing it back to a certain definite sensory stimulus that has been applied here as chief criterion for the concept of H.V. of memory-images.

In contrast to the phenomenon of recurrent sensation it is characteristic that the H.V. of memory-images do not as a rule presuppose a very intensive previous sensory stimulus. They may be called forth by stimulations of everyday life, as, for instance, the visions described in observations 1-3.

Observation 1 (Observer II).—A vision is born: a heap of electrocardiograms, which are seen wriggling on a black surface. Everything is seen very exactly, the typical waves of the electrocardiograms are also partly visible.—Connection: In that same evening, before leaving the laboratory and before turning out the laboratory lamp, I threw an attentive glance on my working table, where the heap of the electrocardiograms was seen. This was the last relatively intense optical perception I had that evening. The image of the vision corresponded exactly to the earlier perception.—Space of appearance: external.

Obs. 2 (Observer III).—There appears upon a dark background an image of an electric switch of the colour of light ivory, looking quite natural and in relief, all shades clearly visible. After one second at the utmost it suddenly disappeared.—Connection: such switches are seen

many times a day, but in a reversed colour-scheme, always a dark switch on a light background. This evening it was for one moment the last optical perception.—Space: external.

Obs. 3 (Observer III).—In the depth of the hypnagogic state during a coughing spell (at the moment when the congestion of blood in the head was at its height) I could see on a grey background the outline of a dock crane.—Connection: this was a reproduced image of a dock crane, seen some hours ago.—Space: external.

A physiologically explainable connection between the subject and these H.V. evidently exists here: certain optical perceptions without any special intensity are reproduced a few hours afterwards in the hypnagogic state, with nearly photographic exactness, in the shape of a H.V. which does not have any psychologically comprehensible contents. The fact that the three previous H.V. belong to the genus of recurrent sensation is evident from the circumstance that these visions can be traced back to an earlier definite sensory stimulus and that they are of a reproductive character.

In contrast to the above instances, the birth of H.V. can also be called forth indirectly, for instance in an associative and reflex way:

Obs. 4 (Observer II).—A fragment of a street car (the upper front quarter) appears in the right part of the field of vision, all details are clearly visible: the blue colour of the car, both lanterns, the signboard with the illegible name of the terminus, etc. The object does not move, the contours of the fragment are somewhat foggy, background of a uniform grey.—Connection: a different street car was seen some days ago, a green one, without lanterns. Before that no street car had been seen for several months. The car fragment seen in the vision corresponded almost exactly to the optical perception that the observer often had many years ago.—Space: external.

By means of a perception of a new, different street car, a memory image of another car, well known from former experience, is reproduced. In obs. 4 a regularity is illustrated which is not rare in cases of associatively caused H.V., i.e. that old memory-images are more predisposed to appear in the shape of H.V. than new ones if a new optical perception with

an associative relationship has exercised a provoking influence on this reappearance.

The associative appearance of H.V. can also be called forth by other modalities of sense, e. g. by acoustic, thermic, and tactile stimuli:

Obs. 5 (Observer III).—The roar of a motor of a car passing by has given rise to a H.V., where a wheelwork was seen, revolving synchronically with the noise from outside.—Connection: an earlier definite perception.—Space: indeterminable.

Obs. 6 (Observer III).—At another time a similar stimulus as that mentioned in the previous obs. gave rise to a vision of a memory-image where, synchronously with the perceived noise, the flame of a candle was seen trembling in the draught.—Connection: an earlier definite perception.—Space: indeterminable.

Obs. 7 (Observer III).—Two rows of teeth appear (life size, seen en face), they are nearly natural, regular, well-shaped teeth without defects. Only teeth are given in the picture, no lips, nor gums.—Connection: immediately before the teeth had been cleaned with cold water and a rough tooth-brush. The teeth which had appeared in the vision strongly resembled a row of teeth often seen in a certain advertisement.—Space: external.

It will be noted that in obs. 4, 5, 6, and 7, somatic stimuli from different modalities of sense called forth such vision of memory-images as had an associative relation to the peculiar character of the provoking stimuli.

As the process of the association itself, owing to the changes in the observer's state of consciousness, nearly always takes place unnoticed, such H.V. may in special cases seem to have been caused synesthetically. For instance, when Anschütz describes a H.V. where, synchronously with the rhythm of speech, there appears a group of dancing figures, not only the interpretation is possible that this is a case of a synesthetically born H.V., but it might also be an unnoticed associatively appearing vision. The H.V. observed and described as a synesthetic phenomenon by Weygandt when he was suffering from conjunctivitis and saw an enlarged picture of an inflamed conjunctiva, also seem to be a vision of memory-image, called forth in an associative way by a somatic stimulus.

B. Synesthetic Visions.—As the conception of synesthetic H.V. given here is based upon a relatively restricted material (26 separate observations by 2 observers), the characterization here set forth is to be considered incomplete. Still, it ought to be of some interest, especially as quite analogous cases do not seem to have been reported in the literature, and as undoubtedly the form of manifestation of H.V. reported here clearly shows the existence of synesthetic elements.

Such phenomena are treated here as synesthetic hypnagogic visions, where a certain sensation in the non-visual modality of sense calls forth an original visual sensation in the shape of a H.V., and where it is possible to determine with evidence that the peculiar features of the provoking stimulus are reflected in the figures of the vision.

Anschütz has pointed out that synesthetic elements are active in certain H.V., even in the case of persons to whom synesthetic phenomena do not otherwise manifest themselves. In spite of the scarcity of casuistry in literature bearing on this subject, it appears as if such phenomena were not, perhaps, so rare. Thus, for instance, two of our three observers showed strong evidence of synesthetic H.V., whereas they show no synesthetic disposition in the wakeful state.

The synesthetic perception is known often to correspond to the primary real facts so precisely, that it is easier to judge of the mode and form of the stimulus by means of the synesthesia, sometimes even easier than through the perception itself, which actually corresponds to the stimulus (Stein). The following examples are intended to illustrate that this state of things can also manifest itself in hypnagogic phenomena.

Obs. 8 (Observer III).—A human right hand appears (grey-white, silhouette-like, with blurred contours), and it is striking that the three middle fingers are spread out and pointing downward.—Connection: the observer's right hand is in a similar position because, owing to the posture of the body in sleep, a moderate pressure (previously unnoticed) is exercised on the three fingers of the right hand which are spread out.—The position of his right hand under pressure corresponds completely to the image of the vision.—Space: indeterminable.

Obs. 9 (Observer III).—An image appears of the right sole in outlines.

—Connection: shortly before he had taken a warm footbath and afterwards walked for some time on the cold floor.—Space: inner.

Obs. 10 (Observed III).—An image appears of the outlines of the naked right forearm and hand.—Connection: congestion of that part of the right forearm which corresponds to the image; the characteristic position of the observer's forearm corresponds to the shape seen in the vision.—Space: inner.

Obs. 11. (Observer III).—A palm appears on a dark grey background (indistinct contours, strikingly larger than life-size, fingers turned upwards).—Connection: when lying with hands crossed under the neck, a considerable pressure is exerted upon the palm of the right hand.—Space: indeterminable.

As the figures of visions 8-11 correspond to the specific position of the subject's body, it is to be surmised that these H.V. as a whole cannot be visions of memory-images, but are independent and original phenomena, a new creation, provoked by tactile and other stimuli of the corresponding regions of the body. Anschütz reports a somewhat analogous example: in the case of a tactile stimulation in the hypnagogic state a light-coloured surface appeared in the visual field.

Observer III, from whom the majority of the synesthetic H.V. reported here are obtained, emphasizes that the H.V. given in obs. 8-11 were entirely different in their characteristics from other hypnagogic phenomena: they are fragmentary figures, silhouette-like, in which certain regions of the body are reproduced (but not in the shape of memory-images); the image is always immovable, with opaque, greyish-white, blurred contours. It is difficult to determine the space of appearance, it is usually inner or indeterminable. Another characteristic feature is the prompt unexpected appearance, so that one always notices the H.V. first, and only later the stimulus necessary to provoke it, and thereby the genetic connection—a state which has been considered characteristic of synesthesia. It is not only the elementary character of those phenomena in which the peculiar features of memory-images are lacking, but also the fact that they are connected with simultaneous or immediately preceding corresponding peripheral stimuli, leads to the supposition that these are synesthetic H.V.

In contrast to those phenomena which may be regarded as primary synesthetic H.V., appearances where the synesthetically caused H.V. is complemented by associatively kindred memory-images are not rare:

Obs. 12 (Observer III).—An image of a standing man is born, seen from behind, dressed in a dark suit. Those parts of the suit which would have touched the support if the man had been lying on his back, are not seen. Only sharply defined white surfaces are visible on those parts of the suit.—Connection: the observer is lying on his back. The white parts of the back of the figure in the vision are about the same as parts of the observer's body, upon which the strongest pressure is exerted when he is lying down.—Space: indeterminable.

Obs. 13 (Observer III).—There appeared for a moment, synchronously with the shaking of the carriage, the outlines of a naked leg in such a position as one is used to see when one's own left leg is crossed over the right—though greatly diminished. The upper part of the leg in the vision is bound by a rubber string, as is usually done in order to obtain congestion.—Connection: owing to the crossing of the legs, the left over the right, there was a congestion in the same region as given in the vision. The part of the leg where it was crossed corresponded to the part bound with the rubber string of the vision.—Space: indeterminable.

Obs. 14 (Observer III).—A distinct H.V. appears, showing the back of a strangely dressed mountaineer in a fixed position, hands and feet held in a peculiar way.—Connection: the observer is lying on a chilly rock. The posture of his body corresponds exactly to that given in the vision, however, the strangeness of the clothing can be traced to a recent perception.—Space: indeterminable.

With regard to obs. 12-14 it appears that the synesthetic elements have become fused with associatively related memory-images. Corresponding to the stimulated regions of the body (pressure on the back, congestion of the leg, stimulation by pressure and temperature on the reverse of the body), associatively kindred memory-images (silhouette of the standing man, the rubber string for provoking congestion, peculiar clothing) have come to join the synesthetic components.

When the question arises how we are to explain the origin of those phenomena, evidently belonging to synesthesia, it would be possible to take into account the so-called corporal schema (Head). It is known that the surface of our body is projected on our cortex through impressions which we per-

ceive from the periphery as well as through intrinsic sensations. The optical, tactile, and cinesthetical "picture" as well as the common feeling of the body, form our corporal schema. Possibly a certain physiological change of the corporal schema which could arise in the hypnagogic state, may cause single parts of our corporal schema (corresponding to the region of the stimulus) to be projected into the consciousness in the shape of hypnagogic visions.

VISIONS OF PSYCHIC CONNECTIONS

Such visions have been designated below as "visions of psychic connections" in which the appearance of the H.V. can be traced back to a certain definite actual mental content, and where a psychologically comprehensible connection can be established between subject and H.V.

Lipps maintains that every representation has the tendency to transpose itself into a full experience, i.e. that every representation has a tendency to become a sensation, a perception. This tendency is usually inhibited. If not, the representation may become a full experience, it becomes a hallucination. The falling away of inhibition is caused, for instance, by expectancy or by suggestion, or by an affective stressing of the tendency (Jaspers). In certain pathological cases Lipps seems to be right, e.g. in delirium tremens, where the patient projects his own ideas as images and voices into the external world as hallucinatory realities.

It has often been pointed out that an analogous phenomenon occurs in the hypnagogic state. Hoche in his hypnagogic state describes such "representations which appear as images and in a very peculiar way spatially." It also seems that Mayer-Gross wants to indicate similar phenomena, when he talks about *Einschlafdenken* and reports a phenomenon *Neigung zur Projektion auch des unanschaulich bedachten in den äusseren Raum*. When Kollarits reports that his own hypnagogic phenomena, as far as their contents are concerned, can be traced back to the "burning vital questions which always tor-

ture me," he evidently refers to the same process, i.e. that there is a psychic connection between subject and H.V., by which the abstract mental contents are reproduced in the shape of H.V. There are reports on similar phenomena by Jéquier, Schultz, Svensson, and others. Hence it is possible in certain cases to speak of a psychic connection existing between the subject's previous mental contents and the contents of the H.V., because the mental contents can be visualized, i.e. transferred into corresponding or associatively related images.

It is possible to speak either of a direct or indirect visualization. The direct visualisation is a phenomenon in which the mental contents transfer themselves immediately into corresponding images. The experiments made by Mayer-Gross together with Beringer and Bürger have yielded the result that it is by no means easy to observe such phenomena in a hypnagogic state, "*weil das Abrollen der seelischen Begebenheiten in diesem Zustand völliger Passivität von dem gerichteten Denken des Wachzustandes so verschieden, so völlig andersartig ist, dass auch dem geübten Selbstbeobachter die Beschreibung nicht mehr gelingen kann. Einerseits werden nämlich die Gedanken, denen angeblich sonst jede Anschaulichkeit mangelt, nach aussen in den Raum, seitlich um den Kopf, vor die Stirn, ins Augenschwarz lokalisiert. Sie steigen vor dem Ruhebett der Versuchsperson auf; im Aussenraum laufen Ansätze von irgendetwas gedachtem.*" It also seems as if Leroy knew the direct visualisation from his own experience: "*Sans qu'il y ait rêverie, il suffit que l'on soit dans l'état de demi-sommeil pour que telle ou telle chose à laquelle on pense, puisse, parfois, isolément apparaître sous forme de vision hypnagogique: une des images qui occupe notre esprit s'illumine soudain sans que toutes celles qui, la dévancant ou la suivant, lui font cortège, aient pour cela changé de caractère; généralement, la vision dure très peu de temps.*" Thus, such phenomena are to be regarded as a direct visualization in which the abstract or concrete mental contents seem to transform themselves immediately into corresponding images, and which the subject can perceive with hallucinatory distinctness.

Indirect visualizations are spoken of when there is a more or less prolonged period of time between the original psychic experience and the process of visualization, as illustrated by the following examples:

Obs. 15 (Observer III).—Suddenly there appears a vision of a button, well formed, upon a dark background (one does not see it, but knows nevertheless that the button must be fastened to some article of clothing). At the very moment the image is born, the button is torn off from whatever it was fastened to, and several ends of torn-off thread remain hanging from the reverse of the button. Nothing is seen which would explain who has removed the button and how it was done. The happening is seen as such: the removal of a button.—Connection: the day before a similar button was examined upon the observer's own coat, to see whether it could be torn off, but it was firmly fixed. He had thought at the same time: although the button sits firmly, yet the coat is somewhat tight here, so it will probably come off "of itself".—Space: indeterminable.

This is a case of an ordinary thought which after a certain time attains visualization in the hypnagogic state. The H.V. begins as a vision of a memory-image (image of the button), but then the part of the vision springs up in which the contents previously experienced by the subject as a train of thought are given in a visualized form (the removal of the button). Thus the earlier mental contents reappear in the shape of a H.V.

Contrary to the *faithful visualization* in which the representation of the object is given as an image of it, an *altered visualization* is often met with, in which the mental contents tending to a visualization, are given as images associatively related to the primary mental contents. Similar to dream-phenomena, an accompanying awareness of significance can manifest itself, which contributes to the understanding of the connection. The example described by Schultz is a case in point (Observer: Kollarits):

Some days ago I was struggling one evening against falling asleep. I lay some time with my eyes shut and thought about different things. It went through my head: what connection would it be possible to find between cyclophrenia and schizophrenia, or rather: what points of contact

did these two diseases show during their whole course. Meanwhile I was getting sleepier and sleepier, the noise from the street below was growing fainter, as if it were coming from afar, but it still reached me quite clearly. I could observe that there were leaps and bounds in the association of my ideas, I could still explain to myself that some hypomaniac and depressive forms also occurred in schizophrenia; suddenly the thinking process ceased entirely and instead a plain appeared before my eyes, I felt as if I were looking from above on a blackboard, upon which two lines intersecting vertically become visible—the system of coordinates, and this geometrical system had a horizontal wavy line: the sinus-line, and a vertical one: the tangent-line, distinctive from each other along both lines—as if they were railway-tracks—two small freight waggons were running. One of them was going from left to right on the sinus-line, the other from the top to the bottom along the tangent-line. They had no label whatever, but I know that the first one corresponded to manic-depressive psychosis, the second (along the tangent-line) to schizophrenia, and that their movement ahead meant the course of both these diseases. The vision disappeared after a short time.

The two following examples illustrate the same phenomenon, i.e. that the psychic experience acts as a primary component, and the corresponding H.V. as a secondary one.

Obs. 16 (Observer III).—A vision appears, showing a large face of a clock with its hand pointing to exactly 3 o'clock. It is accompanied by an awareness that the time has come to get up.—Connection: just before (some 30 minutes) the mental content was present that one has to get up at three o'clock.—Space: indeterminable.

Obs. 17 (Observer III).—A vision of one's own empty shoes appears, seen from above. According to the accompanying awareness, this is to signify that one must put them on and go out.—Connection: shortly before the mental content was present that one will have to go out soon.—Space: indeterminable.

The three preceding observations have the following features in common: there is a psychologically comprehensible connection between the contents of H.V. and the previous actual mental contents of the subject; these actual mental contents, out of which the corresponding H.V. are born, have an abstract character (speculation upon a scientific problem, the train of thought with the resolution "to get up at three o'clock" or "to put on one's shoes"), but during the visualiza-

tion these abstract contents are rendered in a concrete form, whereby such memory-images are used which are associatively related to the contents (two freight-waggon not touching each other, the clock, the shoes). Moreover, it is characteristic that—similar to dream-phenomena—a “symbolic” reshaping of the mental contents manifests itself, and that an accompanying awareness is present, which helps to elucidate the connection with regard to contents that exists between the H.V. and the subject. In order to distinguish such H.V. from dream-phenomena it must be emphasized that these H.V. have not been perceived in dream consciousness, but in the hypnagogic state, and that the observer regards these unexpectedly appearing phenomena with a feeling of strangeness and criticism.

If a question is put about the genesis of the visions described in the observation of Kollarits and obs. 15-17, we must suppose that earlier actual mental contents were connected with cerebral processes which may be reactivated later on, and now, if they reappear during a hypnagogic state of mind, may give birth to H.V.; thus, psychologically, the earlier mental contents appear as the primary or “causative” factor. In case of such visualizing processes it seems as if the psychic component had a “constructive effect”: out of the infinitely great number of our memory-images only certain images (associatively related to the previous actual mental contents) are chosen when creating the H.V., in order to bring forth some definite contents.

In opposition to the above instances, in which the actual mental contents must be interpreted as primary components, and the corresponding H.V. as secondary, we can often find H.V. where the reverse seems to apply, i.e. that a primary somatically caused H.V.—by means of a superimposition of subject’s actual (often affective) mental contents—acquires its contents and “psychic connection” only in a secondary manner:

Obs. 18 (Observer I).—During a railway-journey I sat in a somewhat uncomfortable position and—as I was trying to fall asleep—I supported my elbows on my knees, bending my head forward so far that I could

rest my face on the palms of my hands, and a constant pressure was exercised on my face and eyeballs, which owing to the shaking of the carriage, was steadily increased in a jerky manner. Although I was somewhat tired and sleepy, because of my uncomfortable position—I had given up all hope of falling asleep. Suddenly a fragment of a human face appeared before me: it was a clearly shaped mouth and its immediate surroundings, I clearly noticed an ironical smile and, the mouth being somewhat open,—the tip of the tongue appeared repeatedly. Seeing this malicious mimicry, I at once recognised the railway guard (by the awareness accompanying the vision). It lasted some seconds.—Connection: an hour ago I had had an altercation with the guard, and had felt vexed at the injustice of that official. —Space: indeterminable.

Obs. 19 (Observer III).—A gigantic human right eye appears in the left half of the field of vision, fixing me with a lively, although immovable stare. One feels as if the glance does not only contain reproaches, but even also a certain judicial penetration, as if it wanted to hold a trial. The image of the vision is given in such a way as if one saw one's own right eye in a mirror.—Connection: peculiar situation of a refugee: various unpleasant affective experiences on the same evening. Arrested some hours ago and awaiting trial.—When lying on the right side, a certain continual pressure is being exercised upon the right eyeball.—Space: indeterminable.

In the case of two previous H.V. it seems possible that the somatically caused vision was the primary component, and that the psychological contents have only been secondarily projected on to it. It may be possible that the birth of the H.V. which presents the images of the stimulated part of the body (face and eye), was called forth by means of synesthetic-associative mechanisms; the contents of the affective experiences of the subject, caused by the peculiar situation, are superimposed on the H.V. (which under different circumstances—as a vision of somatic connection—would not have had any contents). Thus the images of the visions obtain a certain new shape, and a psychologically comprehensible connection is achieved. In this connection it is interesting to compare the results of Maclay-Guttman's experiments with mescaline, in which a distinct superimposition of psychic contents becomes evident.

Owing to the frequent presence of the accompanying awareness of significance and to the reshaping of the contents in

a "symbolic" way, the visions of psychic connections can—from the inner viewpoint—be compared to dreams, but on the other hand—from the viewpoint of formal peculiarities (elementariness and fragmentariness of the figures)—they are similar to visions of somatic connections.

In what follows a comparative survey of the chief distinctive marks of vision-types described above will be taken:

HYPNAGOGIC VISIONS CONSIDERED FROM THE VIEWPOINT OF

somatic connections:	psychic connections:
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CONNECTION BETWEEN THE SUBJECT AND VISION:

is physiologically explainable	is psychologically comprehensible
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MENTAL CONTENTS OF THE VISION:

cannot be established	are evidently present
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GENETIC FACTORS:

an adequate sensory stimulus as a genetic factor	an actual mental content seems a genetic factor: continuation or reshaping of preceding actual mental contents in the form of visions
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VISION IS TRACEABLE BACK TO THE PRECEDING:

sensory stimuli: A. To a definite optical perception (visions of memory-images, for instance obs. 1-3). Similarity to recurrent sensations. B. To stimuli from non-visual modalities of sense (synesthetic visions, for instance obs. 8-11). Similarity to synesthetic phenomena.

psychic experiences: For instance obs. of Kollarits and obs. 15-17. Those visions may be compared to dreams as to contents, and to visions of somatic connections as to their formal characteristics (elementariness and fragmentariness of the figures).

As the hypnagogic visions usually have been considered phenomena of a more or less uniform nature (Leroy and others), an attempt has made here to show that there exist some typical forms of H.V., which differ in their substance.

Moreover, as the phenomena of recurrent sensations and synesthesia have been regarded as being of a different substance (Schneider and others), this point of view ought to be valid also with regard to their hypnagogic forms of manifestation, i.e. to the visions of memory-images and synesthetic visions. Thus, such species of hypnagogic visions are described here as must be considered different in substance—not only from a phenomenological, but perhaps also from a genetic point of view.

IV. ON THE DIAGNOSTIC SIGNIFICANCE

The consideration of hypnagogic hallucinations in everyday psychiatric practice may be of differential-diagnostic value, especially if the question has to be decided whether or not any pathognostic significance is to be ascribed to some hallucinatory phenomenon.

The hypnagogic hallucinations afford the only occasion when also a sane person, closely studying himself, can gain at least some conception as to the nature of real hallucinations (Gruhle). If one wants to understand with psychological evidence the statements of some patients concerning their hallucinatory experiences, our theoretical knowledge alone will not help us, but a approximate knowledge of similar phenomena gained through self-observation will rather prove indispensable. In this connection reference is made to reports on self-observation by Hoche, Kollarits, Kraepelin, Leroy, Schneider, Svensson, Trömmel, Weygandt and others.

A spontaneous manifestation of H.V. to persons who as a rule scarcely notice them, may in itself be a symptom of exhaustion, of a toxic state, febrile delirium, or amentia. They then usually disappear with the opening of the eyes (Bumke).

It is not only the manifestation of H.V. that can be a pathological symptom in itself, but the peculiar character of the pathological traits can also show itself in the contents of the H.V. In this respect the contents of the so-called *ängstliche Visionen des Hysterikers* are characteristic: dreaded persons,

such as policemen, the public prosecutor, the hangman, the teacher, suddenly stand in the room; coffins, corpses, ghosts, distorted faces, animals appear, move about, float in the room, climb through windows; persons sit down on the bed. The hallucinations usually change scenically, shift and move (Bumke). Some children see at night, just before falling asleep, some frightening vision, the same every day or nearly every day, through long periods, sometimes months or years (*les visions terrifiantes stéréotypées des enfants*, Leroy).

Schultz regards certain H.V. as "a physiological first step towards pathological hallucination"; he thinks that patients suffering from serious neurotic complaints, even though in all their manifestations of life they cannot be considered pathological, often in their hypnagogic state show a preexistence of such a "pathological mechanism", which, by addition of a certain process, reveals itself as psychosis. Like Schneider, who considers the experiences at the moment of falling asleep to be related to schizophrenia, Schultz regards the bizarre elements of the H.V. as well as their phantastic associations and the complex character spreading itself on to more than one modality of sense, although it seldom provokes the feeling of reality,—as mechanisms akin to those manifesting themselves in pronounced schizophrenia. It has to be taken into account, however, that Schultz's results are mainly based upon pathological material.

Many cases with pathognostic conjectures are set forth with regard to the manifestations of H.V. in certain organic disorders of the brain (postencephalitic states, chorea, narcolepsia), but these results should be regarded as not coinciding (Guyon, Münzer, and others).

A psychodiagnostic importance attributed to the H.V. by writers with psychoanalytic tendencies is not always to be regarded as being of a homogenous nature, as the phenomena there set forth under the name of "hypnagogic hallucination" (e.g. Silberer, Stekel) quite often show the typical characteristics of dreams. We look in vain into the works of these authors for a more detailed characterization of the state of

consciousness in which these sensory experiences have been perceived.

Although real visual hallucinations are exceedingly rare in everyday clinical practice (with the exception of serious organic and acutely-toxic cases), one often hears the patients claim that they have had "visions". In order to be able to interpret the patients' statements and to judge their pathognostic significance, a better knowledge of the different manifestations of the H.V. and similar phenomena in normals would be of the utmost importance. Perhaps it is most important in cases of "visual hallucinations" that the examiner does not so much try to find the pathological element, but turns his attention to attempts to explain the given phenomena by means of normal occurrences. Of course we can but seldom rely on the objectivity of statements made by the patients. We must always bear in mind exaggerations and retrospective falsifications of memory. Also the characterization of the state of consciousness later on is seldom reliable. Often hypnagogic hallucinations and vivid dreams are later considered as visions seen in the wakeful state, etc. The main thing will therefore be to estimate the phenomena under a differential-diagnostic point of view, striving at the same time to ascertain, contrary to the usual assertions of patients—that it is not a case of real visual hallucinations, but only of symptoms without any pathognostic significance. Even if the "hallucinations"—as to contents—are of a typically schizophrenic character, and taking into consideration the view held by Schneider and others, namely that the phenomena of normal persons experienced at the time of falling asleep are related to schizophrenia, we can by no means regard the schizophrenic contents of some visions as surely pathognostic signs, at least not without paying due consideration to the patient's state of consciousness.

Also for the elucidation of a possible hereditary disposition to hallucinations and for investigation into the mutual relations between non-pathological hypnagogic visions and pathological hallucinations a more exact knowledge of the normal hypnagogic phenomena may be of importance. The observation

that the father normally has spontaneous images of recurrent sensations, the daughter only in exceptional states of epilepsy, lends a tangible support to all those suppositions which take into consideration a pathological release of certain phenomena, still within normal limits, by means of a mental disturbance (Schneider).

Furthermore, the question is still open whether, and to what extent, certain constitutional characteristics are reflected in the type of H.V. In this connection it would be worth while to point out a remarkable observation of Goldkuhl's, namely that slightly oligophrenic subsolid personalities (in the sense of Sjöbring) possess a predisposition to "vivid and plastic visual hallucinations". As far as this applies to H.V. of psychic connections, it coincides with our experience, i.e. that subsolidity seems to be a constitutional predisposing factor for the appearance of H.V. of psychic connections. It would be an object for further investigations to find those correlations which might exist between certain peculiarities of constitution and certain types of hypnagogic hallucinations.

SUMMARY

As the hypnagogic visions (H.V.) usually have been looked upon as phenomena of a more or less uniform character, it is the aim of this work to define the limits of some typical manifestations of the H.V., and to characterize them as phenomenologically, perhaps also genetically, different from one another. In order to isolate the H.V. from dream-phenomena, a boundary-line of the hypnagogic state as sharp as possible is drawn. "The beginning of qualitative changes of psychic processes" (when the state of fatigue sets in or is already present) is considered the first line of demarcation. The border line between a hypnagogic state and dreams is marked by the loss of the continuity of consciousness of situation. Accordingly, all such images are regarded as H.V. which are perceived within the limits of the hypnagogic state with closed eyes.—Self-observations (by three healthy observers) were used as

material, 170 H.V. in all. In contrast to those authors who are inclined to make use of such H.V. as can be characterized as "phantastic" phenomena without any especially established connection with the subject, only such H.V. have been selected to form the basis of this work, whose characteristic features can be traced back either to definite somatic stimuli or to definite actual psychic experiences, i.e. which show an evident connection with the subject. On the basis of the peculiar characteristics of this connection a differentiation is made between: (1) "visions of somatic connections" and (2) "visions of psychic connections". The first group consists of H.V. in which the form-elements given in the vision can be traced back to the characteristic features of previous somatic stimuli. The connection which can be established here between vision and subject is physiologically explainable, but does not have any psychological contents. The most frequent form of this group of visions is *vision of memory-images*. They may be considered as a hypnagogic form of manifestation of the so-called recurrent sensations. Another form, also belonging to H.V. of somatic connections, is made up of *synesthetically born H.V.* In contrast to the above, these are not reproductions of earlier optical perceptions, but new creations, whose genesis is caused by stimuli from other modalities of sense; there are also mixed forms, in which the synesthetically born H.V. have become fused with associatively related visions of memory-images.—As contrasted with the H.V. of somatic connections which are devoid of psychological contents, the H.V. of psychic connections possess contents which can be traced back in a psychologically comprehensible manner to certain previous psychic experiences (actual mental contents). The existing psychic connections can be either of a primary or of a secondary nature. In the first instance the psychic experience must be regarded as a primary, the corresponding H.V. as a secondary component. In the second instance the physiologically explainable appearance of a vision of somatic connections must be considered as a primary, and the superimposition of the actual mental contents as a secondary component. Owing to

the frequent presence of the accompanying awareness of significance and to the reproduction of the contents in a "symbolic" way, the visions of psychic connections may be compared to dreams as to contents, and to visions of somatic connections as to their formal characteristics.—Reference is made to the diagnostic significance, which a better knowledge of H.V. can have in certain cases.

ZUSAMMENFASSUNG

Da die hypnagogen Visionen (h. V.) ihrem Wesen nach im allgemeinen als mehr oder weniger einheitliche Phänomene aufgefasst worden sind, wird in der Arbeit die Aufgabe gestellt: einige typische Erscheinungsformen der h. V. unter einander abzugrenzen und an sich als phänomenologisch, möglicherweise auch als genetisch, wesensverschieden zu betrachten. Um die h. V. isoliert von Traumercheinungen betrachten zu können, wird eine möglichst scharfe Grenzbestimmung des hypnagogen Zustandes erstrebt. Als Anfangsgrenze wird dabei „das Einsetzen der qualitativen Veränderungen des psychischen Geschehens“ (bei beginnendem oder schon vorhandenem Müdigkeitszustand) bestimmt. Die Grenze zwischen hypnagogem Zustand und Traum wird durch den „Verlust der Kontinuität des Situationsbewusstseins“ markiert. Demgemäss werden diejenigen Bilder als h. V. angesehen, die innerhalb der Grenzen des hypnagogen Zustandes erscheinen. — Als Material dienen Selbstbeobachtungen (3 gesunde Beobachter), insgesamt 170 h. V. Im Gegensatz zu jenen Autoren, die geneigt sind von solchen hypnagogen Visionen auszugehen, die als „fantastische“, ohne bestimmten Zusammenhang mit dem Subjekt erscheinende Phänomene charakterisiert werden können, sind in dieser Arbeit nur solche hypnagoge Visionen als Grundlage gewählt, bei welchen die formellen oder inhaltlichen Eigenschaften entweder auf bestimmte somatische Reize oder bestimmte aktuelle psychische Erlebnisse zurückführbar sind, also einen evidenten Zusammenhang mit dem Subjekt aufweisen. Es werden auf Grund der Eigenart dieses Zusammen-

hanges differenziert: 1) „Visionen der somatischen Zusammenhänge“ und 2) „Visionen der psychischen Zusammenhänge“. Bei den ersteren handelt es sich um solche h. V., wo die in der Vision gegebenen Formmerkmale sich auf die Eigenart der vorherigen somatischen Reize zurückführen lassen. Der Zusammenhang, der sich dabei zwischen Vision und Subjekt feststellen lässt, ist physiologisch erklärbar, besitzt aber keinen psychologisch verständlichen Inhalt. Die häufigsten Formen dieser Visionsgruppe sind die Erinnerungsbildvisionen, die man als hypnagoge Erscheinungsformen des Sinnengedächtnis-Phänomens auffassen kann. — Eine weitere Visionsgattung, die ebenso zu den Visionen der somatischen Zusammenhänge gehört, bilden die synaesthetisch entstandenen h. V. Im Gegensatz zum Vorigen, handelt es sich hierbei nicht um Reproduktionen früherer optischer Wahrnehmungen, sondern um Neuerzeugnisse, deren Entstehung mittels Reize aus anderen Sinnesmodalitäten veranlasst ist; es kann sich auch um Mischformen handeln, wo die synaesthetisch entstandenen h. V. mit assoziationsnahen Erinnerungsbildvisionen zusammengeschmolzen sind. — Im Gegensatz zu den h. V. der somatischen Zusammenhänge, die psychologisch inhaltslos sind, besitzen die h. V. der psychischen Zusammenhänge einen Inhalt, der in einer psychologisch verständlichen Weise auf bestimmte frühere Erlebnisse (aktuelle Bewusstseinsinhalte) zurückführbar sind. Der dabei vorhandene inhaltliche Zusammenhang kann entweder primär oder sekundär erscheinen. Im ersten Fall ist das psychische Erlebnis als primäres, die entsprechende h. V. als sekundäres Komponent aufzufassen. Im zweiten Fall ist das „physiologisch erklärbare“ Erscheinen einer Vision der somatischen Zusammenhänge als primäres, das Hinzuprojektieren des aktuelln Bewusstseinsinhaltes als ein sekundäres Komponent aufzufassen. Wegen des öfteren Vorhandenseins der begleitenden Bedeutungsbewusstheit und wegen der Wiedergabe des Inhaltes in „symbolischer“ Weise, sind die Visionen der psychischen Zusammenhänge ihrem Inhalt nach mit Traumphänomenen, auf Grund ihrer formellen Eigenschaften aber — mit Visionen der somatischen Zusam-

menhänge vergleichbar. — Es wird auf die diagnostische Bedeutung hingewiesen, die die nähere Kenntnis der h. V. in gewissen Fällen besitzen kann.

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